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THE
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ORIGINAL ARTICLES

THE OCCURRENCE OF ANKLE-CLONUS WITHOUT GROSS
DISEASE OF THE CENTRAL NERVOUS SYSTEM.

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FOR a long time ankle-clonus passed as one of the most certain signs of organic disease of the central nervous system, and some authors even asserted that it did not occur in the absence of such disease. In 1879, however, Strümpell¹ pointed out that clonus occurs with considerable frequency in consumptives, in severe cases of typhoid, and in emaciated, weak patients, without other signs pointing to disease of the nervous system, excepting hyperesthesia of the skin and muscles.

It is the purpose of the present article to point out what conditions may be accompanied by ankle-clonus without other evidence suggestive of disease of the nervous system, to present a few illustrative cases, including one in which an autopsy revealed slight microscopic changes in the medulla oblongata, and to discuss the importance of clonus in diagnosis and prognosis. This is desirable for the reason that the subject is not fully treated in the text-books of medicine and neurology.

The Theory of Ankle-clonus. By ankle-clonus in this article is understood the true ankle-clonus, in which, on continuous upward pressure being made on the sole of the foot, there is a series of rhythmical oscillations in plantar flexion and extension, occurring with a frequency of from five to seven in the second, and continuing for a considerable period, often in fact so long as the pressure is maintained. Cases of so-called false clonus, in which a few irregular

¹ Zur Kenntniss d. Sehnenreflexe, Deutsch. Arch. f. klin. Med., 1879, xxiv, 188.
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contractions take place, are not included. True ankle-clonus is never found in normal persons, and when present is usually associated with exaggeration of the tendon reflexes. It is rarely present in cases showing increased tendon reflexes due to functional conditions (neurasthenia, etc.), but is frequently observed in organic disease of the cord or brain, on which account it has been assigned considerable diagnostic importance. Clonus is also found, but less frequently, in other situations, especially the knee and jaw. In animals a closely analogous phenomenon is encountered in the so-called scratch reflex, so thoroughly studied by Sherrington.² Here in response to a continuous electric stimulation of the skin a series of rhythmical movements of the leg takes place, having a frequency of four in a second. Absolute regularity of the contractions is present in both conditions, and has been shown in the case of the scratch reflex to be due to the presence of a refractory phase, during which stimulation fails to elicit a muscular contraction. The path of the reflex may be assumed to be from the sensory fibers in the gastrocnemius muscle to the lumbar cord, and thence back again to the muscle by its motor nerve. But the reflex is of course more complicated than this, involving coincident inhibition of the antagonistic muscles, and a later contraction of these muscles to bring the foot back to the original position. The close analogy with the scratch reflex, which has been shown to be a spinal reflex, makes it probable that the cerebral cortex is not directly concerned in the production of clonus.

Ankle-clonus in Infectious Diseases Without Gross Lesions of the Central Nervous System. In pulmonary tuberculosis, Strümpell, as already stated, was the first to note the presence of ankle-clonus. He found it of fairly frequent occurrence, especially in emaciated subjects. Longard³ seems to be the only writer to have made an extensive study of the subject, finding it present in 30 of 82 tuberculous cases, but in only 7 of these was clonus associated with a general increase of the tendon reflexes. Six of these 7 were emaciated and febrile, the other was neither. In 8 cases clonus was noticed in well-nourished patients. He makes no mention of the stage of lung involvement, but from the fact that his cases were observed in a general hospital it may be assumed that they were in an advanced stage. Personally I have not met with clonus in incipient tuberculosis, but only in cases in the last stage.

In typhoid fever the reflexes have been more thoroughly investigated, especially by the French. Remlinger⁴ found ankle-clonus in 21 out of 100 cases, but in some of these the clonus was only "suggested." In these 21 cases with clonus the tendon reflexes were increased in 16, normal in 2, diminished in 2, and absent in 1.

² The Integrative Action of the Nervous System, London, 1906.

³ Deutsch. Zeitschr. f. Nervenheilk., 1891, i, 300.

⁴ Rev. de Méd., 1901, xxi, 46.

The plantar reflexes were normal in all. The period of the disease in which clonus was first noted was variable, the phenomenon occurring with about equal frequency in the early stage, at the height of the fever, and during defervescence. It is important to note that clonus was more frequent in the severe cases, indicating a high grade of toxemia, for the mortality in the cases with clonus was 28.6 per cent., almost three times that of the cases without clonus (10 per cent.).

In other infectious diseases, such as septicemia (Case I of this paper), pneumonia, dysentery, cholera, malignant syphilis, the occasional presence of clonus has been noted, but no systematic studies have been made.

The following cases observed by the writer will serve to illustrate the occurrence of clonus in infectious diseases. The first is of particular interest because it is one of the few in which a postmortem examination of the central nervous system has been made.

CASE I.—*Septicemia following sinus thrombosis; marked clonus of ankle and jaw; autopsy; no meningitis nor gross lesions of central nervous system; moderate degenerative changes in pons and small foci of myelitis not involving pyramidal tracts.*

F. E., a female, aged fourteen years, entered the Massachusetts Charitable Eye and Ear Infirmary March 28, 1909, suffering from mastoiditis and sinus thrombosis, for which an operation was performed. There followed an intermittent fever, which continued until the death of the patient, April 15. When seen by the writer, April 12, there was marked emaciation, the head was retracted and stiff, and Kernig's sign was present. There was a marked and continuous clonus of the jaw and of both ankles, and the kneejerks were increased. The plantar reflexes were normal, and there was no spasticity of the legs. Lumbar puncture on two occasions yielded a clear fluid of normal pressure and sterile on cultures. On the fourteenth day the patient had fallen into a condition of stupor. The jaw clonus was less marked, and the ankle-clonus was present on the right side, but only suggested on the left. She died April 15. At the autopsy (Dr. Verhoeff) there was found suppurative mastoiditis, with thrombosis of the lateral sinus at the site of operation, and intense venous congestion and edema of the cerebral pia-arachnoid, but no signs of meningitis; the spinal cord was not examined. There were septic endocarditis of the mitral valve and septic infarcts in the lungs, spleen, and kidneys. There was pus in both pleural cavities. From the spleen the streptococcus was obtained in pure culture.

Microscopic Examination: Unfortunately only the medulla oblongata was available for microscopic study. For the notes the writer is indebted to Prof. E. E. Southard, of the Harvard Medical School: "The positive findings were two in number: (1) A generalized diffuse blackening of the fibers in the white matter

wherever examined, of a sort to suggest curable toxic changes rather than incurably destructive degeneration, and (2) foci of exudative myelitis, in general of an exceedingly mild character, but in one instance striking and associated with alterations in the nerve tissue itself.

"To begin with the focal lesion, we find the meshes of the sheath of the posterior median artery in the posterior median septum densely filled with mononuclear cells, including a few pigment-bearing cells, a small but somewhat larger number of endothelial cells containing mononuclear cells, great numbers of lymphocytes, and a number of plasma cells. The endothelium of the posterior median artery had been largely stripped away and lost. One other small artery in the lateral segment of the bulb was found invested with a slender amount of exudate. The others, including the meningeal arteries were quite free from exudate.

"There is no evidence of spread of exudate into the neighboring bulb tissue. The nerve cells of both nuclei of Goll do not stain properly, but neither do any other nerve cells seen elsewhere look as nerve cells should."

CASE II.—*Severe typhoid fever in a girl, aged eight years; massive hemorrhages on twenty-fifth day, followed by marked ankle-clonus; direct transfusion of blood, with prompt improvement, and disappearance of ankle-clonus in five days.*

B. C., a female child, aged eight years, entered the New Haven Hospital September 7, 1910 (service of Dr. C. J. Bartlett), with typhoid fever. At entrance the knee-jerks were normal. The disease ran a severe course, and on September 25, the twenty-fifth day of the disease, there were two profuse hemorrhages from the bowels. When seen by the writer the next day the child appeared exsanguinated, restless, dyspneic, and thirsty, but was conscious. There was marked and continuous ankle-clonus on both sides, the Achilles and patellar reflexes were greatly increased, but the Babinski and Oppenheim phenomena were both negative and the abdominal reflexes were normal. There was no spasticity. There were no signs of meningitis nor of other disease of the central nervous system. The same day the operation of direct transfusion of blood was performed, with immediate improvement in the alarming condition. The clonus persisted until October 1, when it disappeared and remained absent thereafter. Recovery was uneventful and complete.

CASE III.—*Girl, aged fifteen years; in last stages of phthisis; ankle-clonus five days before death.*

E. K., Russian Jewess, entered the Channing Home for Consumptives October 4, 1903, and died October 9, 1903. Duration of symptoms four months. Physical examination showed an emaciated girl, too weak to sit up. There were signs of extensive consolidation and a cavity on the right side, and of less extensive

involvement of the left lung. There was a typical ankle-clonus on the right side and a slight one on the left. The knee-jerks were increased; the sensation was normal.

CASE IV.—*Girl, aged seventeen years; in third stage of phthisis; ankle-clonus six weeks before death.*

A. E. F., an Irish girl, entered the Channing Home for Consumptives August 31, 1903, with symptoms of three months' duration, and died November 29, 1903. She had lost fourteen pounds in weight, but was still fairly nourished. Temperature, 102°, pulse, 140. The process advanced rapidly, and in a month after admission there was complete consolidation of the right lung and of the left upper lobe. Tubercle bacilli were found in the sputum. Ankle-clonus was found on both sides, with marked exaggeration of the knee-jerks. Four days later the clonus was well marked on the right side, but only slight on the left.

Cases like the foregoing are not uncommon, but heretofore have not been generally recognized. It will be noticed that the clonus may be either one-sided or bilateral, and does not usually persist for more than a few days or weeks. In the writer's experience clonus has been more frequent in the young and in the female sex, but this may be due to the nature of the clinical material.

Ankle-clonus in Cachexia. Sternberg⁵ mentions clonus in weak, emaciated patients afflicted with malignant disease and "senile marasmus."

Ankle-clonus in Various Intoxications. In uremia ankle-clonus is not uncommon, and, as Curschmann⁶ pointed out, may in chronic cases, come on several days before the uremic seizure, thus furnishing a valuable prognostic indication. Lion⁷ also found a marked increase in the tendon reflexes, and sometimes ankle-clonus shortly before the uremic outbreak, though a moderate increase was not uncommon in chronic nephritis in the absence of uremic symptoms. With improvement or recovery he found a return of the reflexes to normal.

During narcosis from ether and chloroform, Goldflam⁸ found ankle-clonus frequently. Strümpell and Sternberg mention increased tendon reflexes in acute strychnine poisoning, but do not state whether clonus was present. Lewandowsky⁹ states that Syllaba and Crocq noted clonus in chronic mercurial poisoning, but the writer was unable to find a reference to the original article. While chronic alcoholism increases the tendon reflexes it does not apparently give rise to clonus in the absence of organic changes.

An interesting state of the reflexes is found after the use of

⁵ Die Sehnenreflexe u. ihre Bedeutung f. d. Pathologie des Nervensystems, Leipzig, 1893, pp. 95 to 97.

⁶ Verhandl. d. Kongress f. innere Med., 1909, xxvi, 341.

⁷ Zeitschr. f. klin. Med., 1903, I, 257.

⁸ Neurol. Centralblatt, 1903, xxii, 1109, 1137.

⁹ Handb. d. Neurologie, 1910, i, 603.

hyoscine (scopolamine) in medicinal doses. Ankle-clonus was noted in from one-quarter to one-half the cases by Hahn,¹⁰ Kutner,¹¹ and Link,¹² and more remarkable still there was a positive Babinski toe sign in a still greater proportion, up to 86 per cent. The Babinski sign appeared in about one-half hour after administration, and after a minimum dose of 0.0004 gm. This production of a positive toe sign indicates a curious selective action on the part of hyoscine not to be found after the use of any other drug, and is one of the few exceptions to the rule that a positive Babinski, when found in adults, indicates organic nervous disease. The tendon reflexes after hyoscine showed no consistent changes, and the muscle tonus was said to be diminished.

Ankle-clonus in Neuroses and Psychoses. In epilepsy, according to Gowers,¹³ ankle-clonus is often to be found immediately after the convulsion, but only for a short time, and Babinski¹⁴ has found his toe sign usually positive at this time.

The occurrence of ankle-clonus in neurasthenia is denied by many authorities, but Oppenheim¹⁵ in his text-book states that it may be found, though rarely. Its presence should make one dissatisfied with the diagnosis of neurasthenia, for in most such cases some organic disease will be found. An instance in point is a case originally reported by Ballet¹⁶ as one of neurasthenia, with ankle-clonus, but shown by the autopsy some years later to have been syphilitic meningitis.

In the case of hysteria there is also much difference of opinion. Most authorities are agreed that ankle-clonus does not occur in hysteria unless there is paralysis, and that it is absent in the common flaccid type of paralysis. In the hysteric spastic paraplegia, with contracture, however, ankle-clonus has been described by many authors, chiefly of the German school. Oppenheim and von Monakow¹⁷ consider it rare, while Strümpell¹⁸ says it is often encountered in this form of paralysis. Babinski¹⁹ claims that when clonus is met with in hysteria it is always due to some extraneous factor, such as organic disease or excessive fatigue. The presence of ankle-clonus in hysteric subjects should therefore always arouse a suspicion of organic nervous disease, which becomes a certainty if the Babinski toe sign is present, for this is never met with in uncomplicated hysteria.

¹⁰ Neurol. Centralblatt, 1911, xxx, 114, 185.

¹¹ Deutsch. med. Woch., 1907, xxxiii, 98.

¹² Zeitschr. f. klin. Med., 1906, lix, 252.

¹³ Epilepsy and Other Chronic Convulsive Diseases, London, 1901, 2d edit.

¹⁴ Rev. neurologique, 1899, vii, 512.

¹⁵ Lehrbuch d. Nervenkrankheiten, V Auflage, 1908.

¹⁶ Rev. neurologique, 1903, xi, 234; 1905, xiii, 732.

¹⁷ Gehirnpathologie, II Auflage, 1905, p. 489.

¹⁸ Lehrbuch d. spec. Path. u. Therap., XIII Auflage, Band iii, S. 615.

¹⁹ L'Encéphale, Paris, 1909, iv¹, 40.

In paralysis agitans, according to Oppenheim, the tremor of the foot may simulate clonus, and very rarely a true clonus may be present.

Bonhoeffer²⁰ and Westphal²¹ have found transitory ankle-clonus, with spastic gait, in acute psychoses in the stage of excitement and loss of weight; Bonhoeffer speaks of his cases as psychosis with anxiety ("Angstpsychosen"), without giving a more definite diagnosis.

Ankle-clonus in Arthritis. It is important to remember that chronic disease of a joint often causes increased reflexes of the corresponding limb, and if the ankle is involved, ankle-clonus is by no means uncommon, apart from any organic nervous disease. In acute articular rheumatism clonus has not been reported, probably owing to the immobilization of the joints by muscle spasm. Jones²² mentions the presence of jaw-clonus when the articulations of the jaw are involved. Clonus may occur in various types of chronic arthritis. Thus the writer has seen it in the gonococcal and chronic infectious types, while Jones emphasizes it in rheumatoid arthritis. The mechanism of its production is not clear, but might be explained on the ground that frequent painful stimuli from the joint put the corresponding segment of the cord into a state of overexcitability, so that the stimulation of the Achilles tendon results in clonus.

Ankle-clonus after Fatigue. Several authors state that ankle-clonus may be found after unusual fatigue, or loss of sleep combined with anxiety, and Auerbach²³ found clonus in 2 out of 39 bicyclists after long distance (50 to 100 km.) races. After long-distance runs, however, the results are different, Knapp and Thomas²⁴ and Oeconomakis²⁵ finding no instances of clonus, but rather a diminution of the tendon reflexes, after "Marathon" races of 42 km. The difference may be due, as Oeconomakis suggests, to the fact that the calf muscles are comparatively little used in bicycling, while in running there is a chance for the reflex arc to become exhausted.

Graphic Studies of Ankle-clonus. The most extensive investigation of clonus by graphic methods has been made by Levi.²⁶ He found that the clonus associated with organic disease showed in the tracing oscillations of equal height and equally spaced, while in the pseudoclonus found in functional diseases and in convalescence from acute infections (only one case studied) the oscillations were of unequal height, giving an irregular appearance to the

²⁰ Seitenstrangerscheinungen bei akuten Psychosen. Psychiatrische Abhandlungen herausgeg. v. C. Wernicke, Breslau, 1896, Heft ii, p. 1.

²¹ Neurolog. Centralbl., 1903, xxii, 12 (foot-note).

²² Lancet, 1902, ii, 1746.

²³ Neurolog. Centralbl., 1905, xxiv, 251.

²⁴ Jour. Nerv. and Ment. Dis., 1904, xxxi, 94.

²⁵ Neurol. Centralbl., 1907, xxvi, 498, 563.

²⁶ Arbeiten. a. d. Neurolog. Institut. a. d. Wiener Universität, 1907, xvi², 27.

curve. In one of his cases, diagnosticated as hysteroneurasthenia, the clonus to the naked eye seemed to be genuine, and only the tracing proved it to be "false." Levi claims that true clonus is always a sign of organic disease, provided that the graphic method has been employed. The string galvanometer of Einthoven has also been used by Salomonson²⁷ in the study of clonus, and he, too, found a perfectly regular curve in the case of organic disease, while hysteria showed, besides the action currents of the clonus, those of voluntary muscle tetanus. These methods appear to offer a valuable way of studying clonus, but the observations have not been extended enough to be conclusive. It is desirable that further studies with them should be made in cases of ankle-clonus without organic disease of the nervous system.

The State of the Skin and Tendon Reflexes. In the class of cases under consideration the skin reflexes may be increased or diminished, but Babinski's toe sign is almost invariably absent, an important distinction from clonus due to organic disease, where it is usually to be elicited. The sole exceptions to this rule are clonus after the use of hyoscine and immediately after the epileptic convulsion, in both of which conditions a positive Babinski is the rule. The same holds true of Oppenheim's sign. The tendon reflexes are usually but not always increased, when clonus is present, whether it be due to organic or functional disease.

Pathological Anatomy of Clonus Unassociated With Organic Disease. Up to the present but three cases have been studied anatomically, viz., those of Strümpell,²⁸ Sternberg,²⁹ and the writer's first case. Strümpell's case was one dying of phthisis, and the spinal cord was found normal, both macroscopically and microscopically. This, however, was in 1873, before the introduction of the finer stains for nervous tissue. Sternberg's case was also one of phthisis, and the spinal cord is said to have been normal on microscopic examination, but no details are given. In the writer's case foci of myelitis were found in the posterior columns in the bulb, as well as diffuse Marchi degenerations. Not too much stress should be laid on the latter, however, for Gay and Southard³⁰ found such diffuse changes in a considerable proportion of cases dying of acute terminal infections. Further studies, including both brain and spinal cord, are necessary before the question of the absence of "organic" changes can be settled.

Explanation of the Occurrence of Clonus in the Absence of Organic Nervous Changes. It will be remarked that practically all the conditions under discussion are accompanied by toxemia, usually of a serious nature. Even in the case of clonus after excessive fatigue there is reason to believe that toxic products are at work. It is possible that the deleterious substances affect only the function

²⁷ Folia neuro-biol., 1910, iv, 1.

²⁸ Loc. cit.

²⁹ Loc. cit.

³⁰ Centralbl. f. Bakt., Parasitenkunde u. Infektionskrankh., 1910, lv, 117.

of the nervous tissue, but it is also not improbable that there are structural changes, such as Edinger,³¹ for instance, has shown to take place in rats after overexertion. Such changes, however, must be capable of complete recovery, for the clonus may disappear quickly, not to return. We are still in doubt as to the exact way in which clonus is produced. If, with Oppenheim, we regard ankle-clonus simply as an exaggeration of the Achilles reflex, we might suppose that the toxic substances rendered the nerve fibers, or perhaps the synapse in the cord, more irritable. The phenomenon cannot be accounted for solely by the removal of cortical inhibition by reason of a lesion of the pyramidal tracts, for clonus is sometimes found in cases of organic disease where these tracts are uninjured, and it may be lacking where they are completely degenerated. The bulbar lesions in the writer's first case are suggestive of the possibility that bulbospinal or bulbothalamal tracts might be of importance in the production of ankle-clonus.

Diagnostic Considerations. The fact that ankle-clonus may appear in so many and varied conditions of toxemia, quite apart from any demonstrable lesion of the central nervous system, makes it necessary to restrict the diagnostic importance heretofore attached to this sign. In the absence of these toxic states, however, it has still a great deal of practical value in the diagnosis of organic nervous disease. The probability of such disease is greatly enhanced if there is in addition to clonus a positive Babinski or Oppenheim sign, as these do not occur in the toxic conditions under discussion, with the exception of hyoscine intoxication and the epileptic attack. The presence of a positive Mendel sign (plantar flexion of the toes on percussing the outer border of the foot over the fifth metatarsal bone), although considerably rarer than the other toe phenomena, appears to be conclusive evidence of organic disease. The complete absence of spasticity and of other signs pointing to organic lesions is also of importance in distinguishing the "functional," or "toxic" cases. On account of the rarity of true clonus in uncomplicated neurasthenia and hysteria its presence should always arouse the suspicion of coëxisting organic disease of the nervous system.

Prognostic Value. In the infectious diseases the appearance of ankle-clonus certainly adds to the gravity of the prognosis, as it indicates a high degree of toxemia, but it does not preclude the possibility of recovery. In nephritis it may be an important sign of the approaching uremic outbreak. The disappearance of the clonus is a favorable sign, except in the severest cases, where it may be only an indication of impending death.

1. SUMMARY AND CONCLUSIONS. Ankle-clonus indistinguishable from the genuine may be found more or less frequently in a variety of conditions, without accompanying organic nervous disease.

³¹ Verhandl d. Kongress f. inn. Med., 1898, xvi, 292.

2. These conditions are: (a) Acute infectious diseases, especially typhoid; (b) chronic infections associated with marked toxemia, especially tuberculosis of the lungs in the third stage; (c) uremia shortly before and during the acute uremic seizure; (d) epilepsy immediately after the convulsion; (e) intoxication from certain drugs, *e. g.*, hyoscine, ether, and chloroform; (f) excessive fatigue; (g) exceptional cases of certain neuroses, viz., neurasthenia, hysteria, paralysis agitans; (h) psychoses in the stage of excitement; (i) chronic articular rheumatism.

3. With the exception of joint disease, a toxic action on the nervous system may be assumed in all these states as the underlying factor in the production of clonus. This is obvious in the case of the infectious diseases and drug intoxications; in uremia, epilepsy, and undue fatigue the presence of toxic products of metabolism may be regarded as probable, though not yet demonstrated, and even in hysteria and neurasthenia the action of toxic products in severe cases cannot be excluded.

4. In the case of articular rheumatism a constant spinal irritation from the inflamed joint tissues is the probable cause.

5. In two autopsies on cases of phthisis, with clonus, no changes were found in the central nervous system. In the writer's case, however, inflammatory exudate was demonstrated about the posterior median artery in the posterior septum of the bulb.

6. Clonus due to toxic states usually may be distinguished from that of organic nervous disease by the absence of spasticity and of other signs pointing to organic disease, and particularly by the absence of the Babinski and Oppenheim toe signs.

7. An exception to the above rule is encountered after the use of hyoscine in medicinal doses and immediately after the epileptic attack, in both of which instances the Babinski and Oppenheim signs may be positive.

8. The occurrence of ankle-clonus is of prognostic value in uremia, preceding at times the acute seizure. Ankle-clonus usually disappears a few days before death, otherwise its disappearance usually indicates an improvement in the patient's condition.

THE RATIONAL TREATMENT OF SURGICAL OR NON-PULMONARY TUBERCULOSIS.

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I DO NOT intend this article to be an argument against the proper use of surgery in surgical tuberculosis. I shall endeavor to show,

however, that in the majority of cases of non-pulmonary tuberculosis surgical interference is but an incident in a course of treatment the most important part of which comes before and after the operation. In other words, in practically no case of surgical tuberculosis can the operator, no matter how skilful, remove all traces of tuberculosis; in tuberculous cervical adenitis, for instance, it is not uncommon to meet patients with large disfiguring scars in the neck and with a history of recurrence of the glands soon after the operation. These patients are recorded on the hospital records as "discharged cured." Only too often subsequent events demonstrate the fallacy of this statement.

During the past three or four years the attitude of many surgeons has undergone a radical change as to the treatment of surgical tuberculosis. While there still remain certain cases in which extensive surgical procedures are indicated, such as in renal tuberculosis, surgeons are coming to realize more and more that their duty to the patient does not end with the completion of the operation and the discharge of the patient from the hospital; they are recognizing the fact that only by constant careful supervision for many months afterward can a permanent cure be obtained. Further than this they are learning that equally careful and constant supervision prior to any surgical procedure will vastly increase the benefits of any operation and in many cases do away with the need of it altogether. This paper is a description of the practical application of these principles as carried out in my clinic at the Massachusetts General Hospital.

In July, 1905, Dr. Joseph H. Pratt, of Boston, started the first "tuberculosis class" in this country. This class consisted of a selected group of consumptive patients who were taught by means of weekly meetings and home supervision how to carry on what was known as "home sanatorium treatment." At the start I became deeply interested in this movement, and soon formed such a class among my own patients. As time went on the number of beds for indigent consumptives in Massachusetts greatly increased, and thus the sphere of usefulness for tuberculosis classes became more and more limited until at the present time in this State one can assign to the tuberculosis class only a small part in the campaign against pulmonary tuberculosis.

This is not the case with surgical tuberculosis, however. There are few beds for children and practically no beds for adults in sanatoria or hospitals in this State where patients with non-pulmonary surgical tuberculosis can receive adequate outdoor hygienic sanatorium treatment of which they are so badly in need. The reasons for this are obvious in that surgical tuberculosis is rarely a danger to the community which has its hands full in caring for its dangerous and infectious cases of consumption. These reasons, though perfectly adequate, render the case of the patient so un-

fortunate as to have tuberculosis of glands, kidney, etc., instead of his lungs a very deplorable one. It became increasingly evident to me that while the usefulness of the home sanatorium movement must become less and less as far as consumption of the lungs was concerned, in surgical tuberculosis it was and will continue to be a potent agent for good.

The hospital authorities have seen fit to call this department which I have built up and devoted to the care of surgical tuberculosis a "tuberculin clinic." This is a misleading name. It is true that with the great majority of my patients I use tuberculin in conjunction with other measures, but in only a few cases would I be willing to attribute to tuberculin all or nearly all of the improvement which has usually taken place. In a certain class of patients with tuberculosis of the genito-urinary tract it has seemed to me that tuberculin is the most important factor in treatment; in the great majority of cases, however, it is undoubtedly a factor, but by no means the most important factor in producing good results. From the start I have confined myself to the use of a bouillon filtrate tuberculin kindly supplied me by Dr. E. R. Baldwin, of the Saranac Lake Laboratory. Other investigators have advocated the bacillary emulsion and certain other preparations, notably bovine tuberculin. My results with the B. F. preparation have been so satisfactory that I see no reason for a change.

Tuberculin is administered once a week according to the well-known rules laid down by Trudeau. The initial dose is 0.0001 to 0.0005 mg., rarely 0.001 mg. This is gradually increased up to 50 to 100 mg. Increase of dosage is gauged by careful observation of clinical signs of a reaction—local, focal, or constitutional. A few patients take their pulse and temperature regularly at home; in the majority of instances this is unnecessary. Constitutional reactions have been exceedingly rare, and in no case has the slightest harm resulted from such occasional reactions while in not a few instances marked improvement seems to have followed a mild constitutional disturbance. It has been my aim to avoid all constitutional reaction by repeating the same dose or decreasing it. I have found it possible to carry most of my patients up to large amounts of tuberculin without the slightest discomfort or disability.

The clinic is held once a week at the out-patient department of the Massachusetts General Hospital; the hospital provides me with a room, necessary equipment, and a nurse. Patients are referred to me from the other out-patient departments, particularly the male and female surgical and genito-urinary departments. Upon the arrival of any new patient, after a physical examination to rule out any pulmonary condition, a card is filled out recording temperature, pulse, and weight. The methods of treatment and reasons for everything that is asked are explained in detail; the patient is then sent to the Social Service Department (without which or its equivalent no such clinic could exist) with the request:

"Please investigate and report to me as to home conditions." This is followed by a personal interview with the social worker taking up the case, in which the exact needs of this individual patient are explained. The chief of the department from whom the patient was referred is also seen and his ideas obtained as to treatment of the local condition. In every case of tuberculous adenitis the patient is sent to the dental department for thorough cleaning of the teeth and to the throat department for tonsillectomy or other procedure if this is deemed advisable. All this takes time. It is often one or two weeks before all these important details can be attended to. At the outset every effort is made to secure the patient's coöperation and to see that he or she understands the reason for everything.

Patients begin to arrive shortly before 9 A.M. Men, women, and children are seen together in one large room. Each patient, on arrival, is given a numbered slip; temperature, pulse, and weight are recorded on the history cards, which are arranged in order at the table where I see the patients. One after another as I call out their names the patients come and talk over with me the details of the past week. If the week has been an uneventful one, and the patient has had no signs of a reaction, constitutional or local, the interview is short; on the other hand, if the patient is not doing well, has lost weight, or is not following out directions it may take some time. Most of the patients I know well and call by their first names; they come to know each other and to enjoy the weekly meetings. I often call the attention of the entire group to striking points coming up in the course of my conversation with individual patients. Frequent consultations are held with the physicians and surgeons of other departments who are looking after the local conditions. The lungs are carefully watched, and whenever the slightest suspicion of pulmonary involvement is found radical treatment usually in a sanatorium is instituted.

WORK VS. REST. Many of these patients keep at their regular work during the entire course of active treatment. While it is advisable and necessary in the majority of instances that all work or school be given up at least for the first two or three months, in not a small number the general condition has been such that it has seemed a useless hardship to impose enforced idleness.

OUTDOOR SLEEPING. During the summer months many patients sleep outdoors; a few sleep out all the year round. The question of fresh air at night is carefully gone into in every case; and in many instances patients are allowed to go to school or to work on condition that they get a sufficient amount of fresh air at night.

LENGTH OF STAY IN THE CLINIC. Patients are urged to attend regularly once a week until the process is cured or arrested. This cannot be done in every case, and, as a general rule, a compromise has to be made. As the local process and general condition improve patients are frequently allowed to come once in two weeks instead

of every week. When the disease is apparently arrested they report once a month or once in two months until a permanent cure is assured.

CLASS OF CASES. The greater number of patients in this clinic are those with tuberculous cervical adenitis; in addition to this there are many cases of genito-urinary tuberculosis, tuberculosis of epididymis, prostate, bladder, tubes, ureter, or kidneys. Other less common cases are those with bone or joint disease, lupus, ocular, and mesenteric gland tuberculosis.

DIET AND DRUGS. If the patient is under weight one quart of milk a day in addition to the usual three meals is prescribed; occasionally olive oil in tablespoonful doses after meals is ordered. Unless the patients are distinctly in need of more nourishment nothing extra in the way of food is ordered, providing that it is definitely ascertained that three really good meals a day are assured. Drugs are rarely if ever used.

STATISTICS AND RESULTS. Since the time that this clinic has been devoted purely to extrapulmonary tuberculosis I have had 209 patients under treatment and observation. Of these 209 patients 50 are in regular attendance every week or every other week, and are therefore not included; 43 patients for one reason or another remained under treatment too short a time to allow of their being considered in this series. The chief causes of this too short a stay at the clinic were:

(a) The presence of pulmonary tuberculosis which necessitated removal to a sanatorium as soon as possible.

(b) The patient's home was too far away to allow of regular attendance.

(c) The home and financial situation were such that the patient was either unwilling or unable to attend regularly.

This leaves 116 patients of whom I can speak with considerable certainty as to results. Each of these has been under more or less constant supervision, coming to report once a month or once in two or three months; the minimum period since attending regularly has been six months; in a large proportion of cases it has been two to four years since they were regular members of this department. These cases are divided as follows:

Tuberculous adenitis	60
Ocular tuberculosis	28
Tuberculosis of kidney	8
Tuberculosis of epididymis	5
Tuberculous tenosynovitis	3
Bone tuberculosis	3
Lupus	3
Mesenteric gland tuberculosis	2
Tuberculous peritonitis	1
Tuberculous salpingitis	1
Tuberculous prostate	1
Tuberculous fistula in ano	1

I have used the terms adopted by the National Tuberculosis Association to denote results. This omits the term "apparently cured" substituting the more conservative one "disease arrested." Of the 60 cases of tuberculous adenitis, which includes young and old patients, those with merely one small broken-down gland and those with extensive bilateral processes on which many operations had previously been performed with no permanent benefit, 46 have had the disease arrested and are now well and healthy in every way, 13 have been markedly improved, while in only 2 instances has the disease progressed despite treatment. There have been no deaths. Of the 28 patients with ocular tuberculosis in some form 9 have had the disease arrested, 17 have been markedly improved, while in 2 cases the process has advanced. Of the 28 remaining cases, which include various other forms of non-pulmonary tuberculosis, 14 have had their disease arrested, 12 have improved, while in 2 the disease has progressed.

These results are by no means startling, although on the whole they are eminently satisfactory when one considers (1) the absolute lack of sanatorium facilities, (2) the comparative lack of adequate home supervision, and (3) the financial condition of most of these patients, which makes it necessary for by far the greater number of the adults to get to work much sooner than would have been the case under ideal conditions.

As stated in the beginning of this paper, I do not attribute to tuberculin alone all or nearly all of whatever improvement has been brought about. It is a judicious combination of proper hygiene, conservative surgery, and tuberculin backed up by individualization in each case and the employment of applied common-sense that has helped these patients in the past and that will help similar patients in the future.

MYOCARDIAL HYDROTHORAX, WITH REPORTS OF CASES.¹

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A COLLECTION of transuded serum in the pleural cavities is a secondary condition, most commonly associated with either cardiac or renal dropsy or the severe anemias, for example, leukemia and progressive pernicious anemia. Not infrequently, hydrothorax also supervenes in chronic dysentery, chronic diarrhea, carcinoma, syphilis, and scurvy. In all of the chronic diseases mentioned

¹ Read before a stated meeting of the College of Physicians of Philadelphia, February 5, 1913.

the condition is in most cases, at least, a late development, often in the course of general dropsy, but such familiar examples are not included in the present discussion. It is also my purpose to exclude from consideration in this paper, hydrothorax dependent upon local stasis due to new-growths of the pleura, lungs, and diaphragm.

The renal group is a large one, and while the cases of hydrothorax that are secondary to chronic parenchymatous nephritis are not considered here, those that come on in the course of chronic interstitial nephritis are unilateral, as a rule, for longer or shorter periods of time, are caused by foregoing dilatation of the heart, and are included with the purely myocardial form. In the latter class both heart and kidney conditions are due to one and the same cause, namely, arteriosclerosis. It is readily conceded that in valvular heart affections attended with general venous engorgement the process may be unilateral for a time in consequence of local obstruction, but this group of cases is also eliminated from full consideration here, although reference will be made hereafter to its relative frequency as compared with myocardial hydrothorax. In short, this paper deals solely with instances of hydrothorax due to myocardial disease, but with some of which chronic interstitial or atrophic nephritis was associated.

The opinion commonly prevails among writers that in cachectic and renal cases, hydrothorax is usually bilateral. But though transudation is, in the majority of cases, bilateral, certain American authors, (Stengel, Osler, and Pepper) have insisted upon the view that it is sometimes unilateral throughout the whole or greater part of its course, for example, in the cardiac group of cases, which may be occasioned either by myocardial changes or chronic valvulitis, and when so is usually right-sided and may be unaccompanied by external dropsy.

CAUSES OF MYOCARDIAL HYDROTHORAX. The association of cardiac disease and unilateral hydrothorax is not rare. This view is confirmed by the observations of Lord,² who found in a series of fifteen cases that six were unilateral and right-sided, of which five were complicated with heart lesions. It is a point of major significance that in myocardial disease the same mechanical influences are at work to bring about a pleural transudate as in valvular disease, principally cardiac dilatation, and more particularly of the right auricle. Moreover, the foregoing fact enables us to understand the reason for the election of the right side of the thorax as the seat of the serous transudate, in cases in which the condition originates primarily in sclerosis of the bloodvessels. Toxic poisoning of the myocardium or of the nerve centres is most probably also a causative factor of first-rate importance in the production of myocardial hydrothorax.

² Osler's Modern Medicine, iv, 848

Again, cases of apparently incipient arteriosclerosis, so far as the peripheral bloodvessels are concerned, may show more marked changes in the small arteries that supply the viscera, the heart, and kidneys inclusive. This has been revealed by recent pathologic studies, and in such instances both the cardiac insufficiency on which the hydrothorax depends and also the urinary phenomena when present are produced by a more or less hidden arteriosclerosis.

On reviewing the literature bearing upon the immediate causes of the cardiac variety of pleural transudate one finds that several recent theories have been advanced and ably championed. A considerable number of writers, among them Cardanelli, Villani, Howe, Lizzatto, and Pepper, attributed the occurrence of right-sided transudation of serum to an old pleural inflammation of low grade, which had so altered the perivascular tissue "that subsequently serous extravasation occurred with general venous stasis that had not become sufficient to cause external or bilateral pleural edema." Stengel³ cites Villani and Peter as suggesting that irritations or inflammations of the liver may extend through the diaphragm to the pleura and thus occasion a combined pleural exudate and transudate.

German writers have also called attention to this variety of the condition in many forms of liver and heart disease, including chronic myocarditis. These may show marked latency so far as general symptoms are concerned, to be followed after a variable length of time by edema of the legs, hepatic enlargement, and finally a left-sided transudate.

More recently, competent observers have noted the occurrence not uncommonly of unilateral or right-sided hydrothorax independently of hepatic disease. Jaccoud first suggested pressure upon the azygos vein and superior vena cava as the cause. Stengel, who arrived at the same conclusion independently, argues from anatomic considerations, that is the relationship of the chest vessels to adjacent structures, that "even a moderate dilatation of the right auricle and cavæ must of necessity exercise considerable compression upon the azygos vein and thus reduce its lumen." Of course, similar conditions do not obtain on the left side of the chest.

More recently still, Fetterolf and Landis⁴ have, as the result of their investigations, concluded that the serous fluid comes from the visceral and not from either the parietal pleura or azygos veins, the outpouring being caused, "so far as the pressure factor is concerned, by dilated portions of the heart pressing on and partly occluding the pulmonary veins." They continue: "Greater frequency on the right side is due to the fact that dilatation of the

³ Univ. Penn. Med. Bull., June, 1901.

⁴ AMER. JOUR. MED. SCI., November, 1909.

right auricle is more common and more easy than a similar condition of the left side, and such dilatation is the only factor needed to cause damming back in the right pulmonary veins. On the left side, in order to include both upper and lower veins, there is needed dilatation of the left auricular appendix and of the left ventricle, with possibly a retrodisplacement of the vertical septum mentioned above, three factors as against one on the right side." In 13 out of my 16 cases of the myocardial form the hydrothorax was wholly on the right side throughout.

INCIDENCE OF MYOCARDIAL HYDROTHORAX. Of 27 cases of hydrothorax due to heart lesions that have fallen under my observation, and of which I have clinical notes, not less than 16 (59 per cent.) were apparently caused by myocardial disease. In 5 of the 16 cases clear and convincing indications of well-pronounced chronic interstitial nephritis were coexistent. These were doubtless instances primarily of arteriosclerosis to which both the myocardial changes and the nephritis were secondary.

In 8 cases only slight evidences of arteriosclerosis coexisted, so that the probabilities are that either the myocardial degenerative and inflammatory lesions were primary or the changes in the blood-vessels of the heart and other viscera were decidedly more marked than in those that are accessible. In 9 cases, however (56 per cent.), the cardiac incompetency which led to the production of the hydrothorax was caused by chronic myocarditis, as will appear evident hereafter.

In none of the 16 cases were the clinical evidences of foregoing valvular sclerosis found. Of course, these figures are too small to base thereon safe inferences, and it is well known that individual experiences differ to a marked degree in relation to special conditions, yet there can be no room to doubt that hydrothorax due to chronic myocarditis is more common than has been supposed. In this connection it is interesting to note that all of my cases occurred in males.

DIAGNOSIS OF MYOCARDIAL HYDROTHORAX. Cases of myocardial hydrothorax are often characterized by extreme latency, particularly during the earlier portion of their course, the only subjective symptoms complained of being dyspnea especially on unwonted effort, and a dry, unproductive cough, which is not especially annoying. This was true of most instances observed by me, although in all the signs and symptoms of chronic myocarditis, for example, cardiac dilatation, with hypertrophy, commonly hypertension, arrhythmia, dyspnea, and in 5 cases, as before stated, those of chronic interstitial nephritis, were present.

Obviously a careful physical examination of the entire thorax would serve to enlighten the clinician, but is, according to my personal experience, often neglected because the hydrothorax which gives rise in a measure, at least, to the dyspnea and cough

is unsuspected. Moreover, my observation confirms the view that a serous collection of considerable magnitude in the right pleural sac may go unrecognized in the hands of a physician who is not fairly expert in the matter of physical examination. The physical signs are the same as those of pleurisy, with effusion, but, unlike the latter, serous collections are never encapsulated.

Osler⁵ points out that postmortem records show how frequently the condition is overlooked. This fact is applicable in a special degree to the cases that arise in the course of chronic myocardial changes after secondary dilatation supervenes, without external edema, and independently of valvular sclerosis. For example, in three of the five cases of hydrothorax which had not been recognized no external edema coexisted until late in the course of the condition.

The principal error in diagnosis then, it has seemed to me, is in the assumption that hydrothorax is not to be expected in cases of cardiac disease in which the signs of chronic valvulitis and external edema are absent. Obviously, not all cases of arteriosclerosis, with hypertension in which dyspnea whether on exertion or otherwise is present, are due to hydrothorax, since this is a striking feature of chronic myocarditis, as a rule, but if on close examination hydrothorax is found to be absent in this condition (chronic myocarditis) it should be recollected that, as pointed out by Janeway,⁶ it indicates marked danger of cardiac insufficiency.

Of the 16 instances of myocardial hydrothorax that have fallen under the writer's observation not less than 5 had been unrecognized, the severe dyspnea having been attributed mainly, at least, to so-called cardiac or cardiorenal asthma and pulmonary congestion. The symptoms and physical signs, however, give a characteristic picture, although it is sometimes difficult to differentiate the cause, chronic myocarditis, from other underlying disease states in which hydrothorax supervenes.

It is not uncommon to meet with cases of myocardial insufficiency that simulate closely those of valvular disease, particularly mitral incompetency, with which may be associated evidence of a mild grade of stenosis. There is, however, not obtainable a clear history of acute articular rheumatism in chronic myocarditis, but commonly of one of the exciting factors that may precipitate secondary dilatation of the heart, such as physical or mental overstrain, an intercurrent febrile affection and the like. Moreover, the apical murmur has a more limited area of transmission in nonvalvular cases, and if the heart be "whipped up" by the use of cardiac stimulants it loses in intensity and may even disappear.

It is said that, as a rule, transudation is not excessive, but in

⁵ Text-book of Medicine, p. 668.

⁶ Jour. Amer. Med. Assoc., December 14, 1912.

two of my cases as much as 2000 c.c. of serum were removed on several occasions, and in one case not less than 6500 c.c. were withdrawn at a single operation. In 15 out of the 16 cases of myocardial hydrothorax, tappings were carried out and no instances of mixed transudate and exudate were met with, although in one case of a right-sided transudate a left sided pleuritis with effusion was associated. While at first sight it may seem trite to suggest that more or less suspicious cases should be needed, there can be little doubt that this simple procedure, which gives us reliable information as to the existence and nature of the process, is not resorted to as regularly as it deserves to be.

COURSE AND PROGNOSIS. While death is inevitable in by far the majority of cases, soon or late, even after marked improvement or apparent comfort has been brought about as the result of treatment, hydrothorax may develop, as my clinical records show at a comparatively early stage of arterial or myocardial disease without recurrence of the condition, if appropriately treated, and life prolonged indefinitely. Thus one of my cases has shown persistent good health for fifteen years following repeated aspirations, and the use of cardiac tonics and stimulants as well as other measures; another for a period of twenty months, and still others for shorter intervals of time.

TREATMENT. The treatment of this form of hydrothorax must have the same objects in view as in the other varieties, and has reference to the removal of the transudate by tapping the chest, and, so far as possible, of the causative condition by hygienic and medicinal means. It is futile, as a rule, to attempt to get rid of the transudate by the exhibition of digitalis and other cardiac stimulants without first withdrawing the fluid by aspiration if it be considerable in amount. I have repeatedly observed that this class of drugs only tends to aggravate the dyspnea without either diminishing the amount of the transudate or increasing, to an appreciable extent, the urinary secretion.

On the other hand, after removing the fluid by means of thoracentesis, cardiac stimulants often take hold and are of signal service in overcoming the dilatation of the heart and preventing a recurrence of the transudate. The myocardial insufficiency in these cases demands a resort to remedies that will strengthen the heart muscle, for example, digitalis, strophanthus and the like, independently of an increased blood pressure, although nitroglycerin should be combined with these drugs if the arterial tension be decidedly elevated.

Rest is a most valuable adjunct in the treatment of the cardiac dilatation to which the hydrothorax is due; it must be, however, absolute and long continued. The use of saline laxatives carried to the point of rather active catharsis—three or four fluid evacuations daily—proved of decided service in a few of the cases.

In five instances of the series herewith reported a salt-poor diet was employed, with favorable effect, reaccumulation of the transudate being thereby noticeably delayed.

Brief notes of my series of cases are here appended:

CASE I.—Col. M. M. J., aged sixty-two years, occupation, Quartermaster U. S. A., consulted me March 25, 1898.

Family previous and social histories negative. The present illness began in March, 1897, with symptoms of neurasthenia and indigestion. He later developed dyspnea and fatigue on effort, and, as his condition did not improve, he was referred to me by his physician.

At my first examination I found the patient suffering from marked dyspnea, a moderate increase of blood pressure, with accentuation of second aortic sound, a dilated heart, and the physical signs of right-sided hydrothorax, the sac being about one-half filled. The urine contained an occasional trace of albumin and a few narrow hyaline casts; specific gravity, 1010 to 1015.

Aspiration followed by complete rest for a period of two months and the use of cardiac stimulants and a non-nitrogenous diet caused the dyspnea and other symptoms to disappear. At the end of six months he again enjoyed good health, which persisted until one year ago, when he died of an acute illness.

CASE II.—F. L. M., male, aged fifty-seven years; occupation, general shipping agent.

Family History. Negative. The patient was subject to tonsillitis during adolescence; occasional mild attacks of rheumatism. Six years ago he was told by a physician that he had "kidney trouble," was ill for one month. Habits good, excepting excessive use of tobacco.

The present illness began six weeks ago, when the patient noticed dyspnea, palpitation, and loss of weight and strength. When I first saw him on March 17, 1908, there was evidence of marked arteriosclerosis, heart hypertrophied, second aortic sound much accentuated, and a moderate amount of free fluid in the left pleural sac, none in the right, and some edema of the feet and ankles. Examination of the urine: specific gravity, 1010; albumin, a small ring; casts, a few hyaline and finely granular; daily amount, 25 ounces. Blood pressure: systolic, 232 mm. Hg. On May 23 the left chest was aspirated and 17 ounces of fluid, having a specific gravity of 1014, were removed. The dyspnea was much improved. The patient left the hospital three days later and no subsequent report on his condition has been received.

CASE III.—H. L. J., male, aged forty-eight years; occupation, fireman, formerly miner.

Family History. Two brothers, a nephew, and a niece died of tuberculosis, otherwise negative. Habits: excessive use of coffee and alcohol for many years.

The patient first became indisposed on August 27, 1908, when he noticed some shortness of breath on exertion, which rapidly increased. When admitted to the Medico-Chirurgical Hospital on October 17, 1908, he complained severely of dyspnea, pain in the left chest, aggravated by breathing and by coughing; mucopurulent expectoration and occasional attacks of vomiting. The patient was cyanosed and an examination revealed an enormously hypertrophied and dilated heart, with weak, rapid pulse; no free fluid in the chest, though numerous fine moist rales were audible over the bases of the lungs. There was marked edema of the feet and ankles. The urine showed a heavy ring of albumin and a few hyaline and finely granular casts. Systolic blood pressure, 180 mm. Hg. No tubercle bacilli in sputum; numerous staphylococci and streptococci present. On October 26 free fluid was noted in both pleural sacs, dyspnea increasing, while pain in the left chest had ceased. Three days later the left chest was aspirated and 21 ounces of cloudy serum, having the characteristics of an exudate, were removed. Cultural studies revealed *Streptococcus pyogenes*. The following day the right chest was punctured and 20 ounces of sterile fluid, having a specific gravity of 1014, were withdrawn. Following this operation the hydrothorax showed no tendency to reaccumulate. On the other hand, the left-sided pleurisy persisted and the exudate was removed on two other occasions before the death of the patient, on November 9, 1908.

Summary of the autopsy findings: Heart hypertrophied and much dilated, especially the right auricle; no fluid in right pleural sac which was normal in appearance; extensive left-sided empyema, with recent pleural adhesions; kidneys showed congestion and diffuse nephritis.

CASE IV.—A. E., male, aged forty-six years; occupation, police officer.

Family History. Father died of heart and kidney disease. Patient has consumed from 15 to 20 "whiskies" daily for the past eight years.

The present illness began in November, 1908, with gradually increasing shortness of breath and marked edema of the legs. Under treatment the patient improved somewhat for a time, but soon after returning to his occupation there was a recurrence of the previous symptoms. When admitted to the Medico-Chirurgical Hospital on January 6, 1910, there was edema of the legs extending half-way to the knees; some cyanosis and marked dyspnea. Heart markedly hypertrophied; second aortic sound accentuated; no murmur. At that time there was no fluid in the chest. Liver much enlarged; slight ascites. A faint trace of albumin, but no casts, was found in the urine. Blood pressure: systolic, 214 mm. Hg. During the stay of twelve weeks the patient showed much improvement, which continued until July 1911, when, following undue

exertion, he had a recurrence of the foregoing symptoms. Again admitted on October 16, 1911, with signs of cardiac dilatation and right-sided hydrothorax. Following removal of this fluid the patient experienced much relief. Since then he has been aspirated at intervals of two months, during which time about 20 ounces accumulate.

CASE V.—B. H. W., male, aged sixty-six years; occupation, manufacturer. Habits good, except for the immoderate use of alcoholic beverages.

On November 30, 1908, the patient came to me complaining of vertigo, dyspnea on exertion, and dimness of vision. Physical examination revealed cardiac hypertrophy and marked arteriosclerosis. Systolic blood pressure, 225 mm. Hg. Ophthalmic examination showed iritis and a retinal hemorrhage near the macula. Urinalysis: albumin, small ring; casts, several narrow hyaline and finely granular. His condition remained about the same until September 5, 1909, when he was taken acutely ill with symptoms of cardiac failure and renal insufficiency. Ten days later free fluid was discovered in the right chest and a moderate amount of transuded serum was removed. This procedure resulted in much relief as to dyspnea, but the patient gradually sank into uremic coma and died three days later.

CASE VI.—V. A. C., male, aged sixty-one years; occupation, railroad inspector.

In December, 1906, I treated the patient in the Medico-Chirurgical Hospital for lobar pneumonia, which was followed by circumscribed, right-sided empyema. After the removal of the exudate, the patient recovered and remained well until January, 1910, when he began to complain of marked dyspnea, unproductive cough, and prostration. Upon his readmission to the hospital (March 5, 1910) I found the heart much dilated, blood pressure moderately elevated, Cheyne-Stokes breathing, cyanosis without dropsy, and signs of free fluid in right pleural sac. Urinalysis revealed a trace of albumin and a small number of narrow hyaline and finely granular casts. On March 15, 48 ounces of transudate were removed from the right chest; March 19, 46 ounces; March 24, 32 ounces were withdrawn. The patient experienced much relief following each operation, but on March 27, he developed facial erysipelas, and died four days later.

CASE VII.—P. R., male, aged forty-two years; occupation, tailor. Moderate use of wines and tobacco; had gonorrhea fifteen years ago.

The present illness began about July 1, 1910, with pain and swelling in right leg, which, however, did not incapacitate him for work until August 15. At this time he began to complain of difficulty in breathing, at times amounting to orthopnea, associated with cough and frothy expectoration. When admitted to the

Medico-Chirurgical Hospital on October 6, 1910, dyspnea was marked, moderate arteriosclerosis present, and the right lower extremity swollen and tender, otherwise no edema. Physical examination showed signs of myocardial changes (dilatation) and right-sided hydrothorax. The transudate (18 ounces in amount) was withdrawn, but in spite of rest and vigorous cardiac stimulation the patient died suddenly three days later.

CASE VIII.—P. L., male, aged sixty-five years. Besides the usual infections of childhood the patient had acute articular rheumatism when aged twenty-eight years.

The present illness began about October 19, 1910, when the patient first noticed dyspnea and palpitation on exertion. On March 16, 1911, these symptoms became more urgent. At this time the heart was dilated, second aortic sound slightly accentuated; no murmur; pulse irregular; lower extremities edematous. Urinalysis revealed a small ring of albumin and a moderate number of narrow hyaline and finely granular casts. Following rest in bed and cardiac stimulation the patient improved somewhat for a time, but early in June, 1911, the symptoms again became aggravated and a moderate right-sided hydrothorax was discovered. On June 15, 16 ounces of clear fluid, having a specific gravity of 1010, were removed. Marked temporary relief followed this operation, but the fluid rapidly reaccumulated, and aspiration was again performed on June 22. Salt-free diet was now ordered and rapid diminution in the general edema followed, but the transudate in the chest reaccumulated, though more slowly. On July 3, 23 ounces were removed from the right chest, and from this time until the date of his death, August 1, 1911, the chest remained free from fluid.

CASE IX.—H. W., male, aged fifty-two years, admitted to the Medico-Chirurgical Hospital on June 15, 1911. Habits: rather excessive use of chewing tobacco and alcohol since early manhood.

The present illness began suddenly six weeks ago, when he awakened one morning in a profuse perspiration and had to gasp for breath. Under treatment by his physician, Dr. J. D. Niles, he improved and felt comparatively well until one week since, when he was again seized with marked dyspnea and vertigo, which persisted. Four days ago he first noticed swelling of feet and legs. On admission I found the patient dyspneic, cyanosed, the heart moderately dilated, physical signs of right-sided pleural effusion, and a small amount of free fluid in the abdomen. Urine negative, except for low specific gravity (1010); systolic blood pressure, 155 mm. Hg. The right chest was aspirated immediately and 10 ounces of transudate were removed. With rest in bed and the use of cardiac stimulants the patient continued to improve and left the hospital twelve days later apparently well. The patient so continued until late in July, when he had a recurrence,

and returned to the hospital, where it was found that the transudate had reaccumulated. The patient left the hospital ten days later in good condition, and there has been no recurrence of hydrothorax.

CASE X.—H. C., male, aged fifty-three years; occupation, liveryman.

Family History. Father and brother died of dropsy.

Previous History. Negative.

The present illness began June 14, 1911, when, following unusual exercise, he noticed weakness and dyspnea. He entered the Medico-Chirurgical Hospital on July 3, at which time a physical examination revealed a dilated heart, an apical murmur, with a small area of transmission, marked arrhythmia, many cardiac impulses, failing to reach the radial arteries. Liver somewhat enlarged. The urine showed a small ring of albumin and numerous hyaline casts; specific gravity, 1025. Systolic blood pressure, 106 mm. Hg.

On July 11 there was some edema of ankles. Two days later signs of free fluid appeared in the right chest. This was removed a few days later, 25 ounces being obtained. The dyspnea was at once largely relieved. Following this there was gradual improvement in his condition, with disappearance of the murmur, and the fluid showed no tendency to reaccumulate. However, on July 29, the patient sat up in bed and suddenly fell over dead.

CASE XI.—M. D. J., male, aged fifty-six years.

Family History. Rheumatism on maternal side. Had severe attack of influenza and rheumatism thirteen years ago; subject to digestive disturbances for many years.

In February, 1910, the patient began to have attacks of angina pectoris. At that time the heart was hypertrophied, arteries markedly sclerotic; systolic blood pressure, 185 mm. Hg. Under treatment the angina attacks became less frequent and gradually ceased, and the patient enjoyed fairly good health until May 29, 1911, when he began to complain of dyspnea and cough.

Physical examination on June 22, 1911, showed cardiac dilatation, arteriosclerosis, a moderate right-sided hydrothorax, and edema of the legs. Urinalysis revealed specific gravity, 1010; albumin, a small ring and casts, a moderate number of narrow and medium hyaline, finely and coarsely granular. As a result of prolonged rest in bed, salt-poor diet, purgation, and cardiac stimulation the fluid gradually disappeared, with marked improvement in his general condition. Since July, 1911, there has been no return of the hydrothorax, and the patient has remained free from symptoms.

CASE XII.—B. E., male, aged fifty-one years. Mother deceased of Bright's disease, and father of heart disease. Nine years ago had ureteral calculus (left-sided) removed. Moderate use of alcohol; tobacco to excess.

The present illness began in October, 1910, with dyspnea, dry

cough, but no edema; as result of treatment he improved and felt well until three weeks ago, when, following undue exertion, the above symptoms recurred in an aggravated form. On November 7, 1911, when I first saw him, there was much distress of breathing, heart dilated and hypertrophied, some edema at bases of lungs and signs of right-sided pleural effusion without general dropsy; systolic pressure, 172 mm. Hg.; arteries palpable. Small albuminuria and the presence of narrow hyaline and granular casts. Patient admitted to Medico-Chirurgical Hospital, where he remained five months at complete rest, with the use of a salt-poor diet, saline laxatives, and cardiac stimulants. Heart stimulants, however, aggravated the dyspnea until transudate had been removed. Later developed edema of legs. After six tappings the fluid failed to recur and external edema disappeared. Patient left the hospital on April 6, 1912, in fairly good general condition. On July 1 received statement from his home physician reporting a sudden recurrence of cardiac dilatation after too much exertion, proving rapidly fatal.

CASE XIII.—T. F. L., male, aged seventy-four years. The patient had acute articular rheumatism when aged thirty-nine years.

The present illness began two years ago, when the patient first noticed arrhythmia associated with dyspnea on exertion. When first seen by me on December 24, 1911, there was orthopnea, legs slightly edematous, vessels decidedly sclerotic, heart action irregular, heart dilated, a faint apical systolic murmur, and marked right-sided hydrothorax, which had been overlooked by the two attending physicians. Urinalysis showed a faint trace of albumin and occasional hyaline casts. Systolic blood pressure, 118 mm. Hg.

After the last of six tappings within three months the fluid showed no tendency to recur and the murmur had disappeared. During this period the patient was given a non-nitrogenous, salt-poor diet, purgatives, and cardiac stimulants. The patient gradually improved and felt well until the last of June, 1912, when he had an apoplectic stroke, which proved fatal.

CASE XIV.—S. J., male, single, aged twenty-one years; weight, 135 pounds; height, 5 feet 8 inches; occupation, laborer.

Family History. Negative. Five years ago was squeezed between two railroad cars, sustaining some internal abdominal injuries. Habits good.

Two years after the above-mentioned trauma was received, dyspnea and abdominal distention appeared. February, 1912, the abdomen was tapped and 20 quarts (patient's statement) of ascitic fluid removed. During the next three months paracentesis abdominis was performed three times.

When admitted to the Medico-Chirurgical Hospital on June 22, 1912, there was urgent dyspnea; cyanosis and arrhythmia; large amount of free fluid in right chest; heart dilated; no murmur

audible; excessive ascites; liver enlarged; very slight edema of lower extremities. The urine was normal excepting the presence of a few hyaline casts. Blood pressure: systolic, 115; diastolic, 100 mm. Hg. On June 24, 10 quarts of transudate were removed from the abdomen. The right chest was frequently aspirated and also the abdomen. Following each operation the patient was much relieved, but both the pleural and ascitic fluids showed a tendency to reaccumulate rapidly. Shortly before leaving the institution a small amount of fluid was discovered in the left pleural sac; this however, was insufficient to necessitate aspiration. The patient left the hospital on August 7, 1912, and died three months later.

CASE XV.—J. L. J., male, married, aged sixty-four years; weight, 144 pounds; height, 5 feet 8 inches; occupation, merchant.

Family History. Negative. About eight years ago had some pulmonary trouble; since then has been spending winters in Florida. Habits good, although he worked hard under nervous tension.

The present illness first manifested itself about two years ago, when slight dyspnea on exertion was noticed. Early in July, 1912, dyspnea became constant, and at times amounted to orthopnea. When I first saw the patient on July 12, 1912, his breathing was very labored and signs of moderate arteriosclerosis and cardiac dilatation were present. At the apex was heard a faint systolic whiff. Signs of bilateral hydrothorax, which had been overlooked, of considerable extent were elicited. At this time slight edema of the ankles was noted; later this became marked and extended to the hips. Urinalysis revealed a small ring of albumin, a moderate number of narrow hyaline and finely granular casts, specific gravity of 1022, and twenty-four-hour quantity, 20 ounces. Systolic blood pressure, 162; diastolic, 140 mm. Hg.

The next day the patient was aspirated and 2 quarts of fluid were removed from each pleural sac. Reaccumulation however occurred, and the operation was repeated on August 3, 13, and 21, with a similar result. Following the last operation, absolute rest in bed was enjoined (owing to extreme nervousness and dyspnea this measure had not previously been practicable), and a salt-poor diet, cardiac stimulants, and saline laxatives were ordered. Under this treatment there was marked improvement; the edema of the legs rapidly disappeared and the chest remained practically free from fluid, and cardiac compensation was reestablished. After a rest in bed of two weeks the patient was permitted a limited amount of exercise; his favorable condition persisted until early in November, when as a result of unwonted physical exertion there was a recurrence of the previous symptoms, with evidences of uremic intoxication superadded. Following the withdrawal of the pleural transudate and the institution of other therapeutic measures,

improvement gradually ensued. The patient's present condition is quite encouraging, although aspiration of the chest becomes necessary at intervals of about three weeks.

CASE XVI.—W. G., male, aged fifty-nine years; weight, 190 pounds; height, 5 feet 8 inches; occupation, shipper in brewery. Father deceased of heart disease; mother of kidney disease. Intemperate use of coffee, tobacco, and alcohol.

Began about ten years ago, with dyspnea, at intervals palpitation and headaches. On admission to hospital on August 13, 1912, he showed a tendency to stupor, was dyspneic and cyanosed, heart dilated with relative mitral systolic murmur, second aortic sound accentuated. Signs of free fluid in right pleural sac. The systolic blood pressure, 185 mm. Hg. The urine contained a medium ring of albumin and a moderate number of hyaline casts; specific gravity, 1008. Examination of the eye-grounds by Dr. J. A. Brophy revealed albuminuric retinitis and recent hemorrhages in both eyes. Removal of the fluid was followed by relief, but patient gradually became comatose, dying four days later. No autopsy permitted.

I am much indebted to Dr. H. Leon Jameson for valuable aid in connection with the clinical records detailed above.

CONGENITAL ATRESIA OF THE DUODENUM.

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INSTANCES of congenital atresia, or complete obstruction of the gastro-intestinal tract, are sufficiently infrequent to warrant the detailed report of individual cases when confirmed by operation or autopsy. The number of recorded cases is by no means large, though no doubt, some are not reported and many pass unrecognized in the absence of postmortem examination. Because of this assumed rarity the condition is not appreciated and the clinical diagnosis is not considered as probable. These malformations are of interest: (1) as a clinical entity, difficult of recognition, and, as to prognosis, practically hopeless; (2) in its clinical and etiologic relationship to spasm and conditions of partial obstruction of the tract; (3) the possible embryologic factors causing such abnormalities are of theoretic interest.

The following case which occurred in my practice is a good example of a complete atresia, with loss of continuity of the duodenum. Baby O.; mother, aged twenty-four years, always well; no miscarriages; two children, aged five and three years respec-

tively. Pregnancy normal; labor apparently precipitated by overwork about two weeks before expected date. Membranes ruptured, with escape of considerable fluid, at 7 A.M., December 11; head engaged in L. O. I. A. by 11 A.M.; child born at 9 P.M., after about one hour of severe pains. Placenta and membranes normal. Though membranes were said to have ruptured in the morning and much fluid escaped during the day it was found in the second stage of labor that a membrane and bag of water preceded the head. This was ruptured, followed by a gush of amniotic fluid. Though not striking at the time, there was evidently an hydramnios, judged by the excessive amount of fluid. This is said¹ to frequently accompany such malformations in the fetus. However, hydramnios is frequently observed, and its occurrence alone would hardly lead one to expect a gastro-intestinal abnormality. Child weighed six pounds eight ounces, and was apparently normal in every respect.

December 12. Child had vomited in the night, had nursed well, and was hungry. Passed some urine, but no bowel movement; continued to vomit at irregular intervals during the day.

December 13. Patient passed slightly colored meconium; nursed well, but continued to vomit; was restless and slept poorly; no urine observed.

December 14. Baby appears emaciated and slightly jaundiced; abdomen distended; vomited large amounts of fluid, containing no bile and in no relation to feeding. Soapsuds enema brought away slightly colored stool. Nursing discontinued and albumin water substituted.

December 15. Child still vomiting; is restless and sleeps poorly; no stools or urine; enema comes away clear. Stomach tube drew off nearly a pint of creamy fluid not bile stained. One could not be sure that all contents were removed, but the washings came away clear and the abdomen was much less distended than before. A diagnosis of pyloric stenosis, with probable complete obstruction, was made, and a hopeless prognosis given. Child rested better for some hours, but became restless during the night and died at 7 A.M.

December 16. A partial autopsy was permitted and only the abdominal condition will be described, since as near as could be determined other parts were normal. On opening the abdomen the distended stomach and duodenum were most prominent, but in normal position, as were the other viscera and omenta. The stomach was dilated to three times its normal size, and the duodenum was much larger than the stomach. There was a definite constriction at the pylorus, which was, however, patent. The duodenum was greatly dilated, but could be traced through its

¹ Little and Helmholtz, Johns Hopkins Hosp. Bull., July, 1905.
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normal course to a blind sac behind the stomach and transverse colon, where it ended, there being no communication or connection with the lower intestine. Rectum and colon were small and

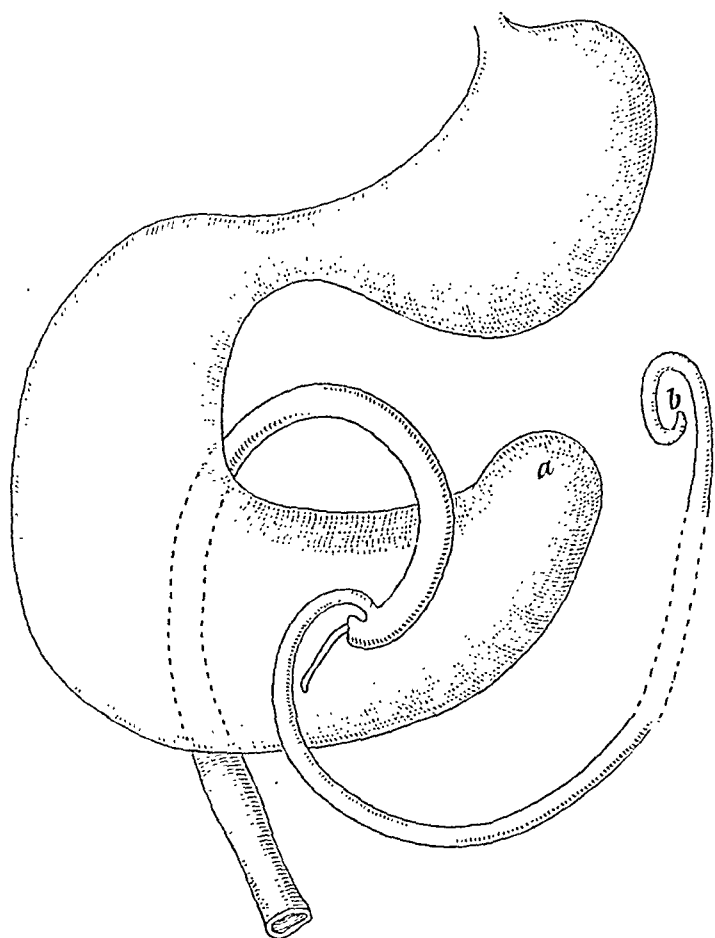


FIG. 1.—*a*, blind end of duodenum; *b*, upper end of jejunum buried in fold of mesentery.

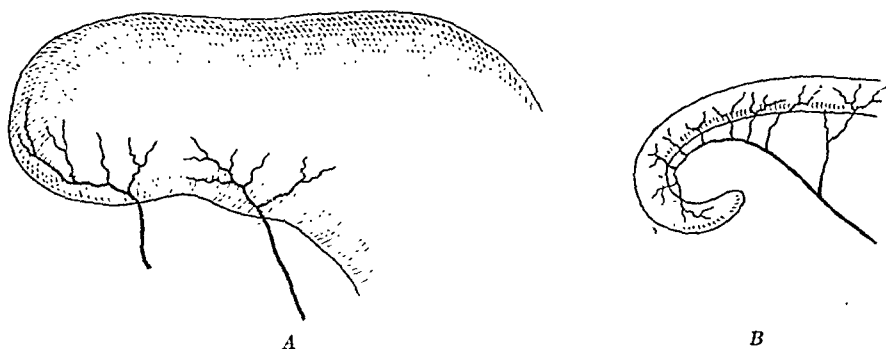


FIG. 2.—*A*, lower end of duodenum with blood supply from superior pancreaticoduodenal artery. *B*, upper end of jejunum buried in mesentery. Blood supply from inferior pancreaticoduodenal artery.

collapsed, the latter extending across the upper abdomen, with the cecum in about its normal position. Appendix long, with normal mesentery. Small intestine contracted and cord-like, being barely permeable. Its mesentery was normal, and no definite constriction was found until reaching the upper end of the jejunum in the region of Treitz's fossa, where it ended in a blind sac covered by a fold of peritoneum. Liver normal in size and position. Gall-bladder distended with bile. Ducts could not be traced to the duodenum. It is probable that no communication existed, as no bile was present in the vomitus or contents of the distended stomach or duodenum, and jaundice was present. We had then a complete atresia, with obliteration of a portion of the tract in the region of the duodenojejunal junction.

Such malformations are not extensively discussed in text-books or even in the literature, except when mentioned as unusual congenital anomalies. There are, however, a few extensive articles giving descriptions of such cases and reviewing the literature, to which I shall refer.²

Defects may be found at any point in the gastro-intestinal tract, but are more common at the following sites and in the same order of frequency: (1) pylorus and duodenum; (2) rectum and anus; (3) ileocecal region; (4) at the attachment of Meckel's diverticulum; (5) the flexures of the large intestine. Atresia and stenosis of the rectum and anus really belong in a different group and will not be considered. Little and Helmholz were able to collect only 27 cases of atresia of the duodenum above the papilla of Vater, including their own. Spriggs adds one of the duodenum, and reports several of the tract lower down. Clogg refers to the following collections of cases: Silberman, with 24 cases of atresia of the duodenum, and 30 of atresia, and 3 of stenosis of the jejunoileum. Schlegel and Braune, with 89 cases of atresia and stenosis of the entire tract, Cordes,³ with 48 cases of atresia and 9 of stenosis of the duodenum. These references are also given by Little and Helmholz, so it is fair to assume they include most of the cases in the literature. Several areas of atresia have been reported in a single individual.

Unless the case is studied with the possibility of such a condition in mind the diagnosis is not made until treatment is hopeless and most often is missed entirely. Many such cases would be classed as malnutrition or spastic stenosis, unless an autopsy confirmed the diagnosis of atresia. Certain symptoms and signs are suggestive, and if carefully studied will enable one to make a correct diagnosis, possibly early enough to warrant surgical intervention. (1) Persistent and characteristic vomiting; (2) constipation and

² Little and Helmholz, Johns Hopkins Hosp. Bull., July, 1905; H. S. Clogg, Lancet, December 24, 1904; N. J. Spriggs, Lancet, January 8, 1910.

³ Archiv f. Pediatrics, 1901.

character of the stools; (3) distention of abdomen, visible peristalsis; (4) anuria, emaciation, jaundice, and other malformations; (5) hydramnios in mother. Vomiting is a constant and important symptom, and may include amniotic fluid, and everything taken by the mouth. It has no necessary relation to feedings, the frequency and amount depending upon the size of the cavity above the stenosis. Bile will be present or absent as the obstruction is above or below the papilla of Vater. Most characteristic is the vomiting of drugs or food given a day or so previously. A stomach tube should be used early in suspected cases, and will demonstrate the size of the viscus. Such findings are often the first indication of an organic stenosis. Vomiting in the newborn is so common that it is often not properly appreciated, but in these cases the duration is short, five or ten days or less, and the progress is rapidly fatal, so that the symptoms should be carefully studied from the beginning. If the stomach is greatly dilated the abdomen will be prominently distended and splashing sounds may be elicited. There may be one or more spontaneous passages of meconium, or an enema may bring away some intestinal contents. In such cases, as with mine, one feels that the condition of the bowels is temporary and that the next stool will be normal. However, such stools rarely contain bacteria, and never, if the obstruction is complete, drugs or digested food. Bile pigments are absent if the obstruction is below the papilla. There may be complete obstipation, which would indicate an obstruction lower in the large intestine. Distention of the abdomen, with visible peristalsis, will be suggestive when present.

Anuria is usually a marked symptom, due to the fact that no fluid is absorbed from the stomach. Emaciation is rapid and progressive, as the child is receiving no nourishment. Daily weighings will show a rapid and regular loss of weight. One might expect to find some form of tetany in these cases, due to the absorption of toxins from the stomach and duodenum; but it was not present in my case, neither is it mentioned in the literature. Jaundice is mentioned in some instances, and was marked in my case. Other congenital deformities might suggest organic obstruction of the intestinal tract in the presence of symptoms. Hydramnios in the mother is said to frequently accompany, but as already stated is too common to alone suggest deformity in an otherwise normal child. Most of the symptoms are exaggerations of those of malnutrition, and often do not attract great attention during the first day or so. The picture rapidly becomes striking, and if one has followed it carefully a diagnosis of pyloric or duodenal obstruction should be made.

More important and also more difficult is the differential diagnosis between (1) spasm of the pylorus; (2) congenital hypertrophic stenosis, and (3) congenital atresia, with complete obstruction.

Spasm of the pylorus may be present shortly after birth, but often does not cause symptoms for some days, weeks, or even months. Usually a certain amount of nourishment passes into the intestine, so the emaciation is not as rapid as is the case in absolute obstruction. The stools show the presence of bacteria and digested food. Hypertrophic pyloric stenosis may give marked symptoms during the first few days, but this also may be delayed for some weeks, and the course is not as rapidly downward. Unless the stenosis forms an absolute obstruction the stools will contain bacteria and digested foods. A palpable tumor would, of course, suggest hypertrophic stenosis. Vomiting is a marked symptom in both the above conditions, but emaciation and malnutrition are slower in their development. In a case of congenital atresia, or complete obstruction, the symptoms must be more marked and rapidly progressive than in those of relative stenosis from spasm or hypertrophy.

The prognosis is bad in all cases of even relative obstruction in the newborn because of the difficulty of nourishing the child, and is practically hopeless in case of complete congenital atresia. Hypertrophic pyloric stenosis is well recognized and discussed in the literature. There are several reports of successful surgical treatment of these cases and a few instances of medical treatment, though in the latter group the diagnosis must remain in doubt. In the complete obstruction or atresia the condition is absolutely hopeless unless the continuity of the intestinal tract can be re-established by surgical procedure. So far as I can find in the literature no such successful operation has been reported, though many have been attempted. There are several factors which are unfavorable to a successful outcome. The diagnosis is rarely made before the child is emaciated and in poor condition to undergo operation; the intestine in the newborn is normally small, rendering an anastomosis difficult at best; the portion of intestine below a congenital stenosis or atresia has been empty and collapsed for months, and perhaps has never been patent. Other obstructions may be present lower in the tract. In my case the distal portion was almost a solid tube, with only a small lumen. Nevertheless in view of the absolutely hopeless prognosis if let alone, operative treatment would be indicated as early as the diagnosis of complete obstruction is made. It is to be hoped that early diagnosis and improved operative technique may save a baby otherwise doomed to starvation. The practically fatal prognosis should be explained to the parents before a surgeon is asked to take the responsibility of operation. Little time should be spent in searching for the obstruction, as the condition of the tract above and below will be sufficient to indicate the sight. Gastro-enterostomy is the operation of choice. If the obstruction is much lower an enterostomy may give temporary relief, and the infant brought into better condition to undergo a final operation.

It is stated that most congenital atresias develop before the fourth month of intra-uterine life, since bile is not found in the distal portion of the intestine. This would fix the time of development before certain important embryologic changes have taken place and to some extent would limit the possible causal factors. Might it not be possible, however, for a certain amount of bile to be absorbed from the fetal intestine into the portal circulation, leaving little trace of its presence. Some of these obstructions might therefore be supposed to occur at a later period. The theories advanced to explain these anomalies are numerous and interesting. The inflammatory theory explains them as being due to adhesions following fetal peritonitis. Ascites has been described in some cases of congenital obstruction, but extensive adhesions are rarely found. Fetal peritonitis, especially in the early months, is not a common finding, and must be limited to the tuberculous or syphilitic forms. It is improbable that a fetus affected with syphilitic peritonitis of sufficient intensity to cause atresia of the intestinal tract would go on to full term, much less develop as an otherwise healthy child. Few if any of these cases have shown signs of congenital syphilis in life or at autopsy. Fetal tuberculous peritonitis is rarely found, and it is hard to believe that only a part of the tract could be involved, leaving no other evidence of the disease. Fetal inflammation may explain isolated cases, but will not cover the majority of them. Pearce-Gould, in 1882, described a case in which the cecum and ascending colon were filled with a plug of cheesy mucus adherent to the intestinal wall. This instance could be explained on the intussusception theory, as advanced by Chiari, who found an atresia 15 cm. above the cecum, with a cylindrical intussusception in the distal portion of the colon. This might explain cases of atresia of the lower bowel more often than is evident at first thought as the necrotic bowel may be disintegrated or absorbed, leaving little proof of the original condition. However, it can hardly explain such anomalies of the pylorus or duodenum. Fetal volvulus, adhesions of Meckel's diverticulum, and an inclusion of a part of the intestine in the closing umbilical ring may cause kinking, occlusion, or atresia of the small or large intestine, but probably do not affect the duodenum. Bland Sutton, in 1889, advanced the idea that most of these malformations were due to errors in development, the most frequent locations of which correspond with the sites of important embryologic events. For example, the most frequent locations of atresia are: (1) pylorus and duodenum, the site of a complicated rotation as well as the outgrowth for the liver and pancreas; (2) the ileum, especially at the attachment of Meckel's diverticulum; (3) ileocecal region, where there occurs a rotation and what is essentially an outgrowth of the sacculated cecum and appendix; (4) the region of the flexures is a less frequent site of malformation and of less importance embryologically. The most

important embryologic changes in the intestinal tract occur in the region of the pylorus and duodenum, but normally result in a patent continuous tube. The duodenum is relatively fixed at the pylorus and at its junction with the jejunum, and the tract undergoes a double rotation about these points. The outgrowths for the liver and pancreas make in all a complicated picture, which, however, normally results in a patent continuous intestinal canal.

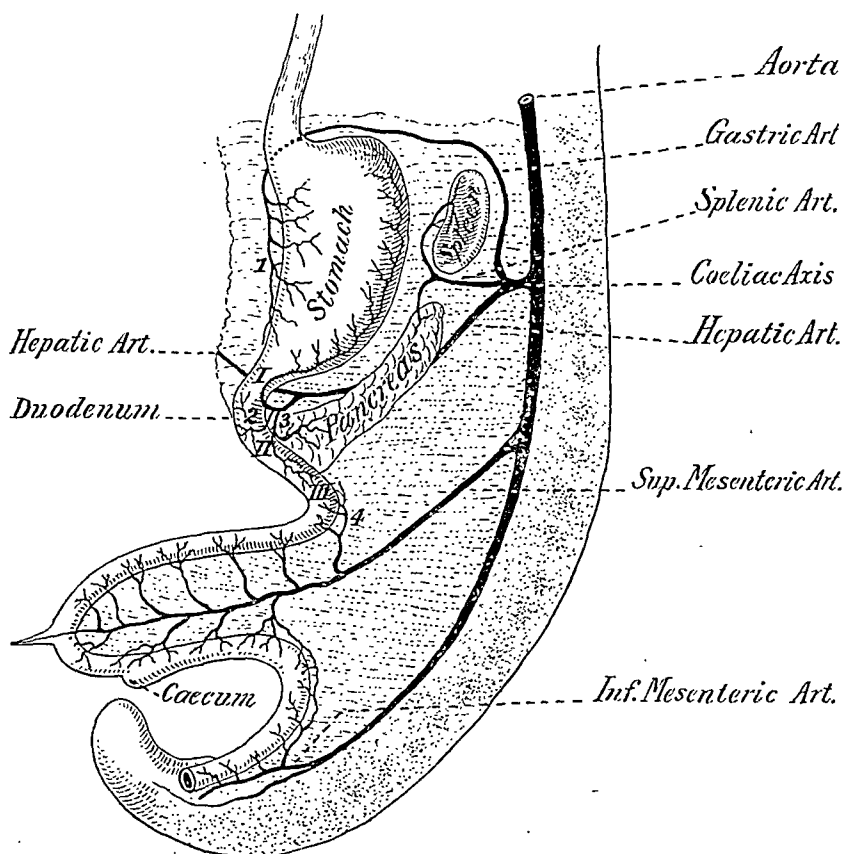


FIG. 3.—Arteries of alimentary tract in human embryo at six weeks: 1, gastric artery; 2, pyloric artery; 3, superior pancreaticoduodenal branch of hepatic; 4, superior pancreaticoduodenal branch of superior mesenteric. I, anastomosis between gastric and pyloric branches of hepatic; II, anastomosis between pyloric and superior pancreaticoduodenals; III, anastomosis between superior pancreaticoduodenal branch of hepatic and inferior pancreaticoduodenal branch of superior mesenteric. (Modified from Kollmanns.)

Likewise at the other sites mentioned the development offers opportunity for deviation from normal and possible occlusion of the canal. However, obstruction does occur at regions where no very complicated event takes place, and must be explained on other grounds. Also some additional factor is required to explain the deviations from normal in the above-mentioned sites. This has been suggested by Joubalay in the idea of congenital vascular anomalies. Little and Helmholtz quote a case of atresia of the

duodenum above the papilla in which there was an absence of the superior pancreaticoduodenal artery, and in their own the superior pancreaticoduodenal, pyloric, and left gastroepiploic arteries were wanting. The blood supply of the fetal gastrointestinal tract below the diaphragm is from three main aortic branches which anastomose freely. (See Fig. 3.)

That of the pylorus and duodenum is from three sources whose branches anastomose freely: (1) a branch from the gastric, which anastomoses with a branch from (2) the hepatic, the pyloric. The hepatic also gives off the gastroduodenal, which divides into the right gastroepiploic and superior pancreaticoduodenal. This latter anastomoses freely with the inferior pancreaticoduodenal from the (3) superior mesenteric. We have then a blood supply from three sources which anastomose freely, and should normally secure efficient nutrition to all parts. Vascular anomalies are not infrequent, and we have here several places where an occlusion or absence of a normal branch might interfere seriously with development of the part, thus leading to partial or complete atrophy. This would be marked by kinking, stenosis, or obliteration of a part, with complete atresia. This is most likely to occur at the pylorus, where branches of the gastric and hepatic anastomose, and at the lower portion of the duodenum supplied by branches of the superior and inferior pancreaticoduodenal. Such vascular anomalies are perhaps most frequent in the duodenal region, but the same possibility exists at many points in the tract. The branches of the vasa intestina tenuis of the superior mesenteric are essentially terminal, and there is little anastomosis between them. Occlusion of one or more of these offers an explanation of atrophy of the small intestine. Whether the fusion of the fetal "intestinal segments" as described by Mall present sites of possible stenosis or occlusion is also an interesting question. A study of the vascular supply to the ileocecal region and its development offer several points where the chain may be broken and an area left without sufficient blood supply.

Such factors then as inflammatory adhesions, volvulus, occlusion by intestinal contents, may explain an isolated case, and this has been apparently demonstrated by careful autopsy dissection. However, there remains a large number not satisfactorily explained by any of these causes. The fact that the majority of these malformations occur at regions where important embryologic events take place renders their explanation as due to developmental error plausible. Together with this we must consider the relation of vascular anomalies as exceedingly important. In fact, I believe these two factors are interdependent, and will explain most of the cases under discussion.

RECOVERY FROM TUBERCULAR MENINGITIS, WITH
REPORT OF CASES.

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McCARTHY in the *Phipps Institute Reports* for 1908 remarks "that evidences of recovery in tuberculosis of the nervous system is as rare as it is common in the lungs." That there is a retrograde process in tuberculosis of the glands, bones, peritoneum, and lungs is, of course, a trite observation.

In the nervous system occasionally tuberculous processes calcify, and meningeal infections become fibrous, quiescent, and finally heal. That such is the case in meningitis of tubercular origin has been a matter of comment by quite a number of writers, notably by Martin, in *Brain* for 1908, who has collected a series of cases in which recovery took place. In all text-books the prognosis is put down as grave or always grave. Dieulafoy mentions but one case that recovered, but he evidently had not scanned the literature thoroughly, because in his own country at the time at which his book was written there were records of at least six or seven cases of undoubted tubercular meningitis followed by recovery. But even the most optimistic must agree that it is always best to tell the family of one stricken with this disease that the outlook is practically hopeless; nevertheless, one must do so guardedly, and follow out certain lines of rational treatment, to be detailed later, in the hope that the lesions may be limited to the cortical membranes of the brain, without exudation of fibrin or purulent matter, and may not extend into the ventricles.

There are, of course, several meningeal diseases closely simulating tuberculosis, and these must be considered in several ways. These are, notably: (1) Quinke's disease, in which there is simply an excess of cerebrospinal fluid, chiefly in the ventricles, not produced by microorganisms and not infectious; (2) influenzal meningitis, simulating it closely, (3) and the meningismus of typhoid. Hereditary syphilis in the young, too, may resemble meningitis of tubercular origin. From the fact that Quinke's disease, which is not of parasitic origin, and therefore probably not toxic in the character of the serous exudate, can simulate true meningitis, it is evident that simple pressure within the ventricles and hence to the skull may cause nervous symptoms, chiefly cephalalgia in both disorders. In meningitis the added poisons and the multiple tubercles massed in nerve trunks and fibrous purulent exudate add much to the pathology and to the gravity of the prognosis.

A typical case of influenzal meningitis is the following: A young grocer, aged twenty-seven years, married, father of one healthy

child, was one evening suddenly seized with a violent headache. This did not yield to any of the ordinary headache remedies, so that by morning morphine was required. Then it was seen from the retraction of the neck, intense pain, retracted belly, *tâche cérébrale* and Kernig's sign, fever, photophobia, and delirium, that meningitis was present. Accordingly, a lumbar puncture was done and 70 c.c. of clear liquid were drained off. This contained a fibrin clot, lymphatic cells exclusively, and no organisms. The headache immediately disappeared, Kernig's sign and rigidity of neck did so after ten days. He gained weight and resumed business. Two months afterward a second attack necessitated another puncture. He then had double vision on looking down and marked abduction of the eyes; jerking of the eyeball was demonstrable. Photophobia, increased knee-jerks, plantar flexion of the toes, *tâche cérébrale*, rigidity of the neck on the right side appeared. At this time headache did not seem so intense, and there was not so much fever. In removing 35 c.c. of fluid the double vision and fulness of the head disappeared during the operation, and the patient became markedly better. The fluid was limpid, clear, but contained some minute bacilli, probably influenzal. A guinea-pig injected with the fluid recovered. In twenty days all symptoms of any disorder promptly disappeared, save some stiffness of the neck. This was probably a case of influenzal meningitis, with lymphocytosis, cured by lumbar puncture and urotropin, which was freely given. There was no history of syphilis in the case, and the Wassermann test was negative.

The following is the history of a case of tubercular meningitis with recovery:

J. S., aged fifty years, linen draper, was admitted to St. Timothy's Hospital with every symptom of meningitis, from which he had suffered for four or five days. He had had such an intense headache that he begged to be shot, and indeed a revolver in his room had to be removed for fear that he would do so. When admitted he was delirious and had a retracted neck, scaphoid belly, and *tâche cérébrale*. A lumbar puncture was done under chloroform and 80 c.c. of fluid were withdrawn. He was a very tall man, measuring over six feet four inches, but was far from robust. In each apex there was evidence of tuberculosis, which from his history had existed for some time; in every way his history was that of one who had a low-grade phthisis for ten years. The present attack came on with violent vomiting and unendurable headache, also pains in his arms and legs. Kernig's, Oppenheim, and Babinski's signs were all present markedly. Pupils were contracted and rigid. On attempting to flex his neck after the lumbar puncture all the major joints flexed, and he groaned.

The lumbar puncture was easily performed, the fluid spurted out, and was quite bloody, due to the puncture of a small vein. This fluid contained three acid-fast bacilli, which in view of the presence

of tuberculosis of the lungs were assumed to be tubercle bacilli. No animal injections were made. A cytodagnosis was not attempted because of the admixture of blood. His pulse was 70; respiration, 26 and jerky; temperature, 99°. His leukocytes numbered 6200; red cells numbered 4,200,000; hemoglobin, 75 per cent. His urine was bloody, and contained albumin and casts. Blood pressure: 128 systolic; 88 diastolic. Marked improvement followed the withdrawal of the fluid. His spastic symptoms slowly receded. His mind became clear in a few days and his headache disappeared. He was given forced diet and urotropin, 30 grains a day. After three weeks' stay in the hospital, to the amazement of all, he suddenly got up, asked for his clothes, and went home. He then had some rigidity of his neck and some evidences of Kernig's phenomenon. After two years he is able to conduct his business and has no evidences whatsoever of any meningitis. In this instance the fact that the patient was an adult and long infected with a low-grade tuberculosis no doubt contributed much to his recovery.

Perhaps the most interesting case of recovery after tubercular meningitis is that reported by Rumple (quoted by Martin), who exhibited at the Aertzlichen Verein, Hamburg, the brain of a boy who died of phthisis. At the age of nine the boy had an acute attack of meningitis, in which there was retraction of the neck and hyperesthesia, absence of knee-jerks, bilateral optic neuritis, ptosis, and palsy of the external recti. Lumbar puncture gave a fluid in which tubercle bacilli were found. The boy, who was treated with repeated lumbar punctures, recovered, and though for some months was dull and stupid, he eventually retained his normal mental condition and was able to keep pace with other children of his age at school, while all physical signs had disappeared. Four years his health continued good, he then developed a tubercular abscess in the axilla, followed by phthisis; death took place eight years after the onset of the meningitis. At autopsy it was found that the membranes over the fissure of Sylvius on either side of the brain were thickened and glued together, but miliary tubercles were no longer visible. Not only was there a confirmation during life of the presence of tubercular meningitis, by the finding of tubercle bacilli, but also post mortem, at which the site of the old infection was discovered and definitely identified. Martin sums up the following requirements to be met in making a diagnosis of tubercular meningitis followed by recovery:

1. Clinical evidence of tuberculosis elsewhere in the body and history of exposure.
2. Differential count of cells in the spinal fluid (meaning an excess of lymphocytes).
3. Presence of tubercles in the choroid.
4. Tuberculin reaction.
5. Demonstration of bacilli in the fluid by staining, inoculation, and culture.

6. Postmortem examination after recovery or long remission and death by some other agency.

If tuberculosis of the meninges be but a local manifestation of a generalized infection (miliary tuberculosis) then the likelihood of recovery is of course minimized. That it is likely under such circumstances, is evidenced by cases reported by Lunn, (1) Dujardin-Beaumetz (2), Thornallas (1), and Brooks (2), in all of these tubercles were seen in the choroid, indicating a generalized infection. Tuberculin reaction, of course, confirmed the diagnosis, but it does not of necessity prove that there may not be some other remote latent infection which is the cause of the reaction. Postmortem examination and clinical diagnosis of tuberculosis elsewhere are, of course, convincing confirmation that the disease is tuberculosis.

In the case of a young woman, recently under the care of the writer, who had severe retractions of the neck, with pain, photophobia, increased knee-jerks, *tâche cérébrale*, tuberculous apex, bilateral pleurisy, high fever, and definite history of exposure to tuberculosis in her home, lumbar puncture revealed nothing and did not alleviate symptoms a particle. A later development of iritis and arthritis of the elbow compelled a revision of diagnosis to rheumatism of the spine, pleura, joints, and eye, showing that mere dependence upon the previous existence of a latent tuberculous lesion for confirmation was misleading and not dependable. Cytodiagnosis is also misleading. Porat reports cases showing that it may be valueless. Forbes, who examined 80 cases, 70 being verified by autopsy or by finding tubercle bacilli, found 51 had an excess of lymphocytes, 5 had an excess of polymorphonuclears; in 4 the proportion was equal. In tuberculosis of the brain not communicating with the meninges the fluid was normal. Goggia found an excess of lymphocytes in a meningococcus infection. Mutzner concludes, from a study of a series of cases with postmortems, that a lymphocytosis is not by any means diagnosed, and reports cases with an excess of the many nuclear forms of leukocytes.

In 797 cases collected by Martin for the London Hospital of unconfirmed tubercular meningitis, 16 (or 2 per cent.) recovered. In Vienna 1369 cases were reported in which recovery took place in 6 (or 4.4 per cent.). Thus in a total of 2166 cases, 22 (or about 1 per cent.) recovered. These, of course, were diagnosticated from mere clinical symptoms. Barlow, also quoted by Martin, states that if the tuberculous process be limited to a part of the surface of the brain there is a possibility of recovery, but if the disease, becomes generalized so that besides the invasion of the pia mater there is an extensive meningo-encephalitis, with or without hydrocephalus, the chances of recovery are practically nil.

McCarthy in several *Phipps Institute Reports* found frequent evidences of healed tuberculosis of the nervous system in subjects that had finally died of phthisis.

TRUE CASES.

Case.	Autopsy.	Bacilli found.	Tuberculosis elsewhere in body.	Cytodiagnosis.	Tubercles in choroid.	Clinical diagnosis.	Tuberculin.	Tuberculous history.	
Treyhan.	None, recovered	Yes	None	Yes	None	..	Choked disk.
Henkel, 17 yrs.	None, recovered	Yes	Yes	
Gross, 20 yrs.	None, recovered	Yes	Yes	Excess polys.	..	Yes	Developed phthisis 8 months after.
Stark, 44 yrs.	None	Yes	None	Yes	Optic neuritis.
Barth, 3 yrs.	None	Yes	None	None	None	Recovered in 6 months.
Stiles.	None	Yes	None	..	None	Yes	Recovered after decompression.
Stiles.	None	Yes	None	..	None	Yes	Recovered after decompression.
Alanzino.	None	Yes	None	Yes	..	Yes	Recovered in good health, 6 months.
Tedeschi, 14 yrs.	None	G. P. Yes	None	Yes	..	Yes	
Jemma, 3½ yrs.	None	Yes	None	Yes	..	Yes	After 3 years, good health.
Gareiso, 8 yrs.	None	Yes	None	Yes	None	Yes	Well 12 months after.
Claisse, 30 yrs. }	None	Yes	None	Yes	Satisfactory recovery.
Abramc.	Yes	Yes	Old tubercles found.
Dufour.	Yes	Yes	Old tubercles found.
Vaquez-Digne.	..	Yes	Yes	Yes	..	Yes	
Rossini.	..	G. P. Yes	Yes	Complete recovery.
Janssen, 19 yrs.	Yes	G. P.	Yes	Meningitis 3 years before death from phthisis.
Politzer.	Yes	Yes	Old lesions and new lesions, 3-year interval between attacks.
• Schwalbe.	Yes	Yes	Both died of diphtheria.
Schwalbe.	Yes	Yes	Evidence of old tubercles found at autopsy.
Carrington.	Yes	Yes	Died of psoas abscess.
Leube, 24 yrs.	Yes	Yes	Died of phthisis and recurrent meningitis. Old tubercular lesion of brain found from previous attack.
Riebold, 6 yrs.	None	G. P. Yes	Yes	574 c.c. drawn in punctures.
Rumpel, 17 yrs.	Yes	G. P. Yes	Yes	Yes	Died of phthisis 4 years after recovery from meningitis.
Lunn.	None	Yes	Yes	Meningitis followed by recovery.
Dujardin-Beaumetz.	None	None	None	..	Yes	Yes	Recovery; diagnosis based on choroid tubercle.
Thornallas.	None	None	Yes	None	Yes	Yes	Tubercles seen in choroid; disappeared on recovery.
W.T.Brooks, 4 yrs.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	..	Autopsy showed old healed meningitis; subsequently died after a long period.
Pitfield, 55 yrs.	None	Yes	Yes	Yes	None	Yes	None	Yes	Recovery, 3 weeks; old tuberculous lesion of the lungs.

I am able to append 29 cases of undoubted tuberculosis, mostly collected by Martin, in which recovery followed and 8 others more doubtful. In 10 autopsies confirmed the early diagnosis. In 18

tubercle bacilli were detected and in 5 of these guinea-pig inoculation confirmed the diagnosis. In 4 cases, tubercles of the choroid were seen. In 7 demonstrable tuberculosis elsewhere was noted.

In view of the fact that recovery can take place in perhaps 1 in 200 cases, steps should be undertaken actively to facilitate such a possibility. The patient should be put in a quiet, airy, dark place and kept as free from annoyance as possible. Lumbar puncture should be performed at once. The writer had a case, a boy, aged five years, from whose spine 40 c.c. of fluid were removed every other day for two weeks, with marked amelioration in the symptoms. Forced feeding through nasal tube, with milk and eggs, should be done. Morphine administered for pain and as a sedative, if respiration is not embarrassed thereby, and because free formaldehyde is found in the spinal fluid after the ingestion of urotropin the latter drug should be given freely. I have found, after giving it for one day, that formaldehyde can be detected in the fluid with iron and sulphuric acid; and because Raw has reported recovery in two cases in which tuberculin was used, I would advocate one or two injections of this remedy.

One case was most skilfully operated on by Dr. George Müller, who decompressed and punctured the left lateral ventricle, withdrawing about four times the normal amount of fluid, the child ultimately dying of respiratory palsy, having lived for three weeks after the diagnosis had been made and gaining five pounds by forced feeding. Why decompression is not fraught with better results in this disease is probably due to the involvement of the ventricles. The unrelieved distention is due to the choking of the canal leading from the third to the fourth ventricle.

AN INTENSIVE STUDY OF THE EPIDEMIOLOGY OF PELLAGRA. REPORT OF PROGRESS.¹

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PART I.

I. GENERAL PLAN OF THE WORK. Although the Thompson-McFadden Pellagra Commission will continue its work in the field

¹ From the Thompson-McFadden Pellagra Commission, New York Post-Graduate Medical School and Hospital.

during 1913, it is considered advisable and warranted to set forth at this time in a brief preliminary report certain results of the epidemiological study made in 1912.

It was decided that an intensive study of the disease as it occurred among the population of a limited area would yield more valuable epidemiological information than a more superficial investigation over an extended area, conducted by correspondence and by brief studies in a number of different localities. No such intensive epidemiological study within a small area seems to have been previously undertaken in pellagra, while much data gathered by the more general methods are already available in the literature.

For the collection of data a blank booklet was prepared, covering points considered of possible significance regarding the patients themselves, their families, their residences, and the neighborhood in which they lived. In order to secure these data, each patient was visited one or more times in his or her own home.

In this preliminary report only summarized data will be included. The detailed epidemiological data for each case, and certain more intensive studies made in selected localities within the county, will appear in the report to be issued on completion of the investigation.

The problem immediately before the commission in all its work was the etiology of pellagra and not its symptomatology or therapeutics, except as these subjects might throw light upon the essential nature of the disease. In view of the essential importance of diagnosis in our work, the conservative position was taken that a positive diagnosis would be made only when the characteristic skin lesion was evident or its earlier presence could be definitely ascertained by the testimony of patient and physician, though this requirement might, and ultimately did, exclude from our records cases which in all probability were suffering from pellagra without showing evidences of its cutaneous manifestation.

II. ACKNOWLEDGMENTS. It is not practicable to make personal acknowledgment in each case to the many physicians to whom we are under great obligations for their interest and coöperation. The Spartanburg County Medical Society supported us in all our work, and we wish to express our high appreciation of its active part in furthering the investigation. Our only way of approaching patients was through their local physicians, and in no case did we find anything but the most ready coöperation on the part of the physicians, while many actively associated themselves in the work at a considerable expenditure of time and effort. In the more intensive studies in selected localities, which will appear in a future report, opportunity will be given us to make acknowledgment of these special services.

We are indebted to Dr. J. W. Babcock for the privilege of consulting with him from time to time during the work, and for many special services, especially for data concerning pellagrins admitted

to the State Hospital for the Insane from Spartanburg County and for pathologic material collected at autopsies in that institution.

To Dr. J. A. Hayne, secretary and health officer of the South Carolina State Board of Health, we are under obligations for his interest and coöperation in our investigations, and particularly for furnishing from his office vital statistics concerning pellagra.

III. THE TERRITORY SELECTED. Spartanburg County is situated in the northern or Piedmont section of South Carolina. It is forty miles long in a north-south direction, thirty miles from east to west, and contains 762 square miles. Its surface is hilly and broken by a network of small streams and by four small rivers which, with their tributaries, flow across the county in a south-easterly direction, one of these rivers forming the county line on the south. The elevation above sea level at Spartanburg, the county seat, is 875 feet. To the northwest the slope is upward, the north-west corner of the county being situated at the foot of the Blue Ridge Mountain range, while to the south and east the elevation becomes somewhat lower than at Spartanburg, but with no precipitate fall, the whole county thus resting upon a plateau about 700 feet above sea level.

TABLE I.—Population Spartanburg County Census 1910.

		Total.	One year.	One to four years.	Five years.	Six to nine years.	Ten to fourteen years.	Fifteen to seventeen years.	Eighteen to nineteen years.	Twenty years.	Twenty-one to forty-four years.	Forty-five years and over.	Unknown.
Total population	M.	83,465	2,733	10,091	2,370	8,852	10,402	5,710	3,878	1,870	26,239	11,161	159
	F.	41,719	1,425	5,167	1,171	4,490	5,270	2,840	1,903	893	12,822	5,652	86
Native white— native parents	M.	41,746	1,308	4,924	1,199	4,362	5,132	2,870	1,975	977	13,417	5,509	73
	F.	56,536	1,918	6,842	1,587	5,834	6,742	3,874	2,576	1,254	17,677	8,149	83
Native white— foreign parents	M.	28,472	991	3,526	793	2,969	3,464	1,907	1,230	642	8,820	4,063	47
	F.	28,064	927	3,316	794	2,865	3,278	1,967	1,296	642	8,857	4,086	36
Foreign-born white	M.	309	5	28	8	29	31	27	8	6	111	54	2
	F.	150	2	15	6	11	12	14	3	2	55	30	
	F.	159	3	13	2	18	19	13	5	4	56	24	2
Black	M.	203	..	1	..	1	4	6	7	5	98	80	1
	F.	136	3	5	6	5	64	53	
	F.	67	..	1	..	1	1	1	1	..	34	27	1
Mulatto	M.	21,944	637	2,675	635	2,445	3,018	1,486	1,098	506	6,910	2,467	67
	F.	10,893	335	1,338	299	1,244	1,489	762	530	236	3,289	1,335	36
	F.	11,051	302	1,337	336	1,201	1,529	724	568	270	3,621	1,132	31
Indian	M.	4,466	172	544	140	543	607	316	189	99	1,441	409	6
	F.	2,065	97	288	73	266	302	152	84	38	593	169	3
	F.	2,401	75	256	67	277	305	164	105	61	848	240	3
Chinese	M.	4	1	1	1	1	
	F.	1	
	F.	3	1	1	1	1	
Japanese	M.	2	1	1	
	F.	2	1	1	
	F.	1	1	
	F.	1	1	

The annual mean temperature, as recorded at Spartanburg, is 60° F. While the winters are mild, killing frosts are apt to occur from November to March inclusive, and the normal mean temperature for the months of December, January, and February is about 42° F.

The total population of the county is 83,465. Spartanburg, with a population of 17,517, is the only city in the county, the remaining population (65,948) being distributed upon farms, in cotton-mill villages, and among eleven small towns, only two of which have over 1000 inhabitants. The density of population, as a whole, is 109 per square mile; for the rural population (that is, outside of Spartanburg City) it is 86.5. While in South Carolina, as a whole, the negroes form 55 per cent. of the total population, in Spartanburg County the whites predominate numerically in the proportion of somewhat over two whites to one negro—there being a white population of 57,055, and 26,410 negroes—the percentage being 68.4 per cent. whites and 31.6 per cent. negroes. The distribution of the population of the county by race, nativity, age, and sex, according to the United States Census of 1910, is set forth in greater detail in Table I.

The chief industry, and almost the only industry conducted upon a large scale, is that connected with the cotton mills. There are about twenty-eight cotton mills in the county, each mill supporting its mill-village. These mills give employment to approximately 10,000 operatives, representing about 4000 families, and a total mill-village population of about 20,000. As the mill operatives are whites exclusively, it follows that something over 35 per cent. of the white population of the county is found in the mill-villages and is supported by the cotton-mill industry. The mill-village population contains no foreign element, but is drawn altogether from the general native-born population of South Carolina, North Carolina, Tennessee, Kentucky, Georgia, and other nearby States. An effort is made by the mill operators to secure families with the maximum number of individuals capable of employment as operatives. The income of the mill workers ranges from about 75 cents per day to \$2 or even more, averaging about \$1.25 per day.

The chief agricultural pursuit throughout the county is cotton culture, though in recent years more and more land has been turned over to corn and other grain crops. The average value of farm lands, \$36.04² per acre, is considerably above that found in many sections of the Southern States.

IV. PREVALENCE OF PELLAGRA IN THE COUNTY. Altogether, 282 cases of pellagra were studied in detail during the period the commission was working in the county, that is, from June 1 to

² United States Census Bureau.

October 15, 1912, and these 282 cases are the basis for the greater part of our study. For the purposes of certain special lines of inquiry, such as the history of pellagra in the county, the geographic distribution of the disease at different periods, the sequence of cases in different local areas, and the possible increase or subsidence of the malady with regard to both frequency and virulence, records were secured of cases known to the physicians of the county, but which had died or moved beyond the county limits. It should be said also that the 282 cases on our list as present in the county in 1912 represent the minimum figures for the county in this period.

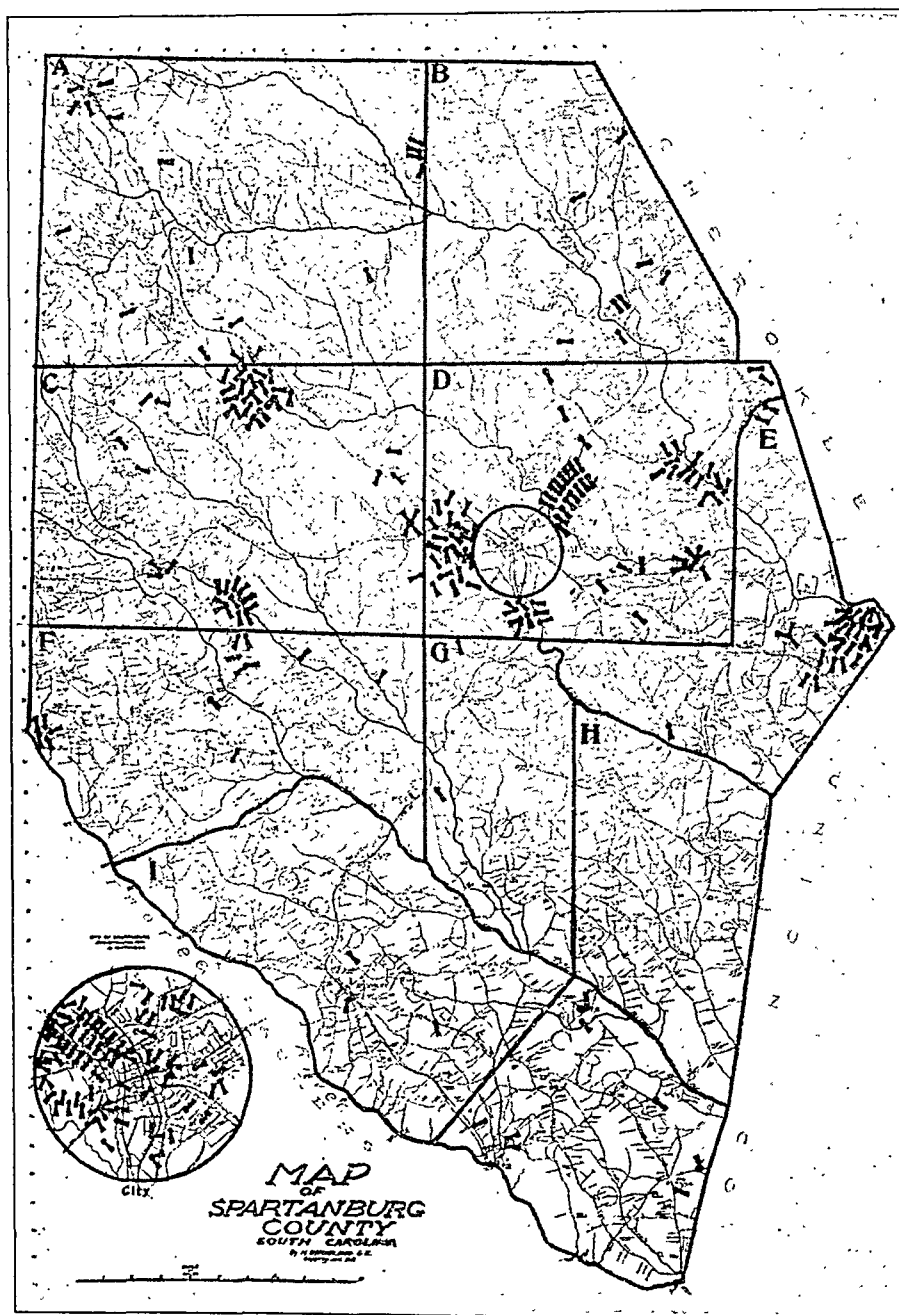
Accepting 282 as the minimum number of cases, we have in Spartanburg County, in 1912, a minimum morbidity rate for the population, as a whole, of 0.35 per cent. or 35 cases of pellagra for each 10,000 of the population.

Including 94 additional cases of which we secured definite knowledge in the county in 1912, but were not able to visit, usually because of their early death or their commitment to the State Hospital, the total number of cases in the county becomes 376, or 44.9 per 10,000 of population. We believe this rate represents very nearly the actual prevalence of pellagra in 1912 in the territory studied.

In view of the fact that this rate is considerably higher than has previously been reported in any single territory of like area, it should be distinctly understood that in no other territory in the United States has so intensive a study been made and pellagrins so thoroughly sought out. Abundant evidence was gathered that the disease is at least equally prevalent in adjoining counties of South Carolina and in certain parts of adjoining States. Furthermore, in Lavinder's extensive compilations of statistics of pellagra in 9 Southern States, 4 States show a greater number of cases than does South Carolina, and 2 States a higher rate per 10,000 of population. Referring to Spartanburg County, Lavinder justly recognizes the exceptional interest displayed by the physicians of the county in the disease, and considers his reports from this county to be exceptionally complete. He was able to get reports of 226 cases up to the beginning of 1912. Our more intensive search, confined to the one county, discovered a total of 398 cases prior to 1912. The difference of 172 cases might be considered surprisingly small were it not for the unquestionable fact that the reports obtained by Lavinder from Spartanburg County were exceptionally complete. There can be no question that the excessive number of cases for Spartanburg County, which appears in both Lavinder's figures and ours, represents more complete returns, and not a greater prevalence of pellagra than is present in other localities from which reports are less satisfactory.

V. GEOGRAPHICAL DISTRIBUTION OF PELLAGRA WITHIN THE COUNTY. In order first to investigate the possibility of any geographical inequality in the distribution of the disease within

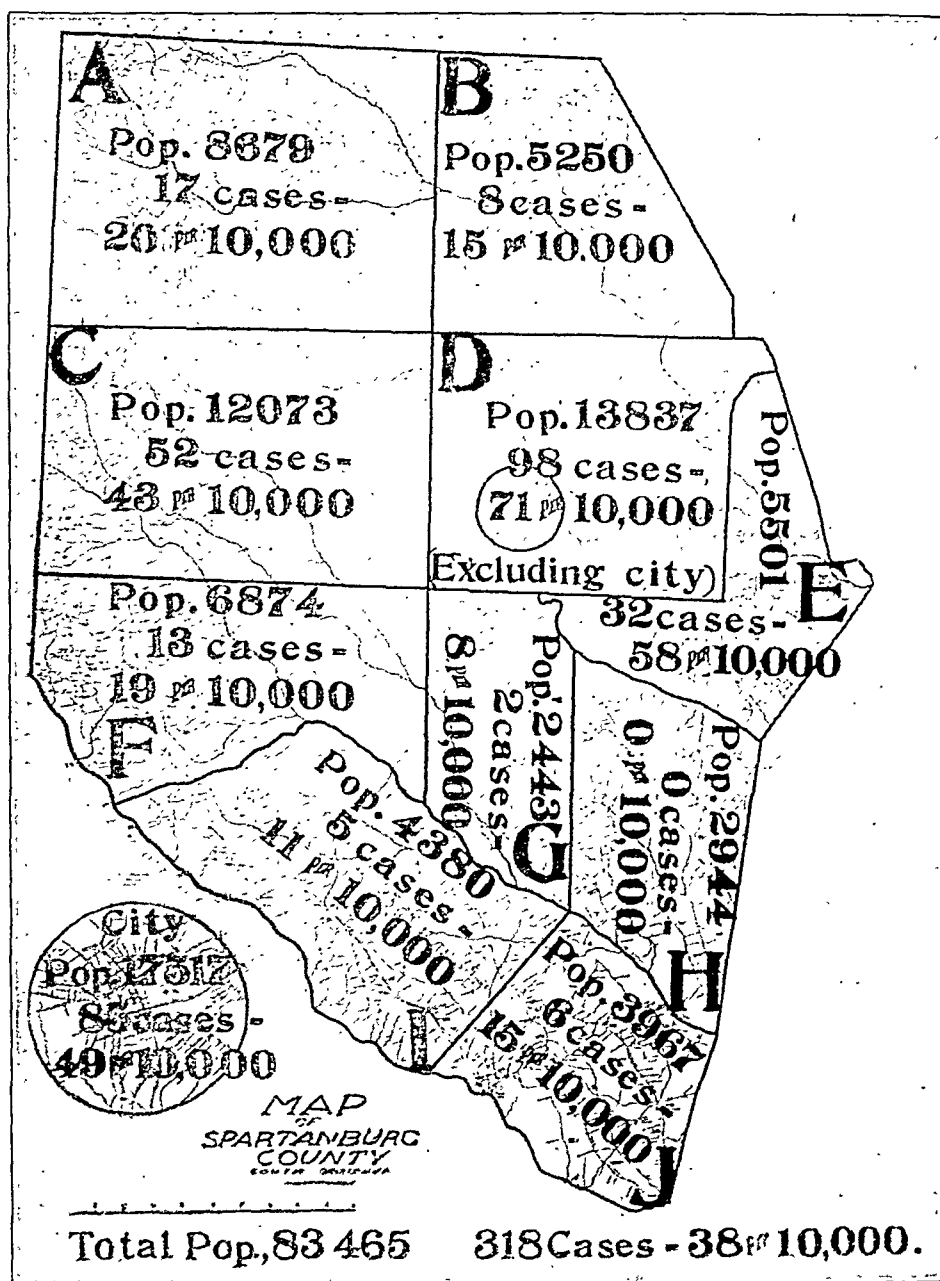
the bounds of the county itself, we have considered the incidence of the disease in each of its ten townships separately.



MAP 1.—Geographical distribution of cases in county and city of Spartanburg in 1912.

By referring to Map 2 it is seen that the township rate per 10,000 of population ranges from no cases in township H to 71 cases per 10,000 of population in township D. It is noteworthy, further, that the three townships C, D, and E, stretching across

the middle of the county, give rates of 43, 71, and 58 cases respectively, or a combined average of 55 per 10,000; while townships



MAP 2.—Distribution of cases by townships with rate per 10,000 of population.

A and B to the north and F, G, H, I, and J to the south give 20, 15, 19, 8, 0, 11, and 15 respectively and a combined average of only 14 per 10,000.

The incidence rate of pellagra within the city of Spartanburg

was 49 per 10,000, considerably lower than the total rate (58) for township D, in which it is situated. The combined average rate of townships C, D, and E, exclusive of Spartanburg City, is 58 against only 14 in the remaining townships.

The population of the county may be still further divided geographically into three parts: (1) the rural population; (2) the mill-village population; (3) the urban population of Spartanburg City. The rural population is found upon the farms and in eleven small towns, one of which has 1880 inhabitants, another 1101, and the remaining nine from 100 to 500 or 600.

Approximately one-fourth of the population of the county live in the cotton-mill villages. There are twenty-eight of these villages in the county, their individual population ranging from about 200 to about 2000. Within the city of Spartanburg there are two

TABLE II.—Rural, Mill-village, and Urban Distribution of Cases by Townships.

Township.	Total population.			Rural population.			Mill-village population.			Excess in mill-village over rural population.
	Population.	Cases of pellagra.	Rate per 10,000.	Population.	Cases of pellagra.	Rate per 10,000.	Population.	Cases of pellagra.	Rate per 10,000.	
A	8,679	17	20	8,179	13	15	500	4	80	65
B	5,250	8	15	4,650	7	13	600	1	17	4
C	12,073	52	43	9,173	17	20	2,900	35	121	101
D ^a	13,837	98	71	7,504	21	28	6,333	77	120	92
E	5,501	32	58	2,751	8	29	2,750	24	87	58
F	6,874	13	19	6,174	8	13	700	5	71	58
G	2,443	2	8	2,443	2	8	0	0	0	
H	2,944	0	0	2,944	0	0	0	0	0	
I	4,380	5	11	3,580	3	8	800	2	25	17
J	3,967	7	18	2,967	4	13	1,000	3	30	23
City	17,517	85	49	(14,567 ^a)	(43 ^a)	(29 ^a)	2,950	42	142	113
County	83,465	319	38	50,365	83	16	18,533	193	104	88

mill-villages, with a joint population of approximately 2950, the remaining 14,567 constituting the city population proper. Such a distribution of the population affords an opportunity to carry farther the analysis of the geographic distribution within the territory of each township by considering separately the prevalence of the disease among the rural, urban, and mill-village population respectively. The results of this analysis are shown in Table II and are graphically displayed by Chart 1.

With one exception, in each of the eight townships with a mill-village population, the prevalence of pellagra among the mill-villages is markedly in excess of its prevalence among the rural population, this excess ranging from 17 per 10,000 in township I to 101 per 10,000 in township C, and reaching even a still higher

^a Exclusive of city.

^a City population exclusive of mill-village.

figure (113) in the city of Spartanburg. In the county, as a whole, the mill-village population shows an excess of 50 per 10,000 over the total county average and of 88 per 10,000 over the rural districts alone. The apparent exception presented by township B, in which the excess among the mill-village population was only

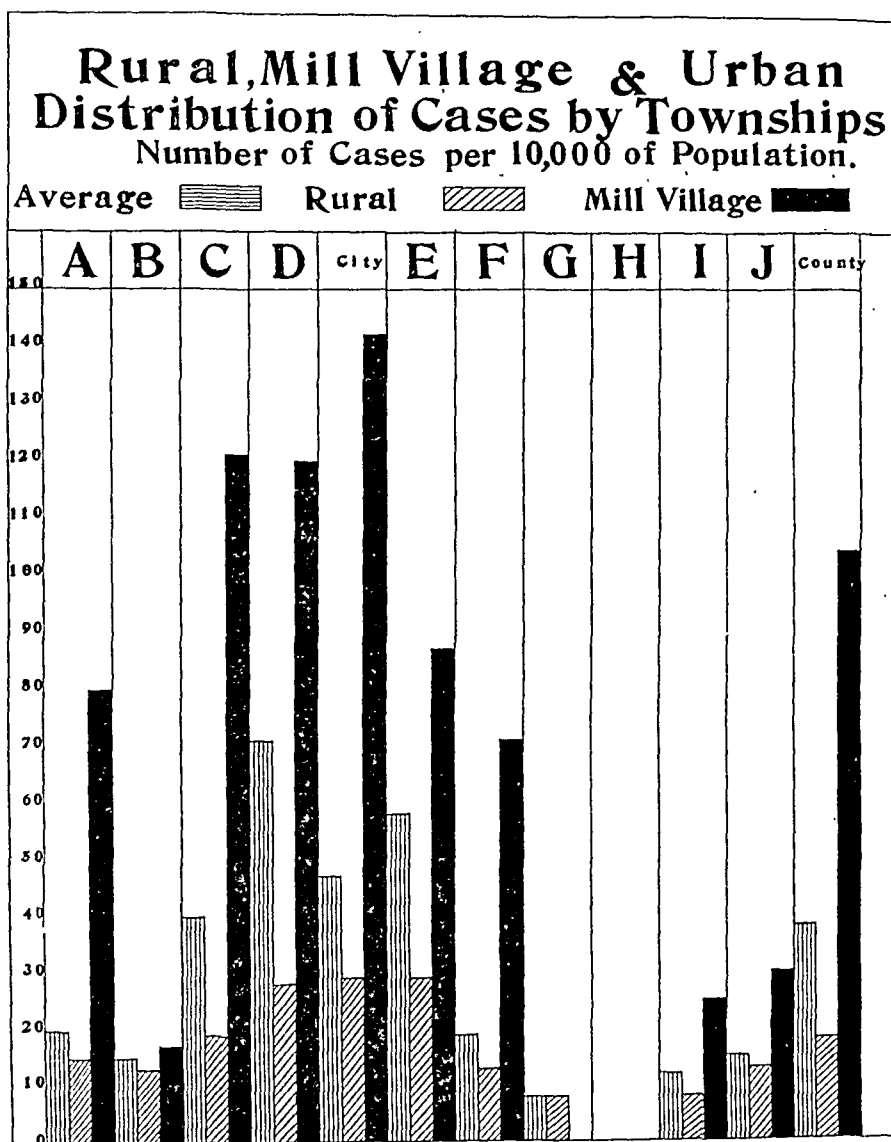


CHART 1.

4, disappears in view of the fact that the one mill in that township had been in operation only a month or so. The rate per 10,000 in the urban population of Spartanburg City, exclusive of the mill-village population of the city, is about equal to the combined rate among the rural population of townships C, D, and E, exclusive

of their mill-village population, while the mill-village population in Spartanburg City (2950) shows 142 per 10,000, the maximum rate in our figures.

Excluding both urban and mill-village population, and considering the rural population alone, we find that the three townships C, D, and E still show a prevalence of pellagra twice that of the remainder of the county, the combined average rural rate for these townships being 24 per 10,000, while for the rural population of the remainder of the county it is only 12.

There are two factors which may possibly offer an explanation of this difference. In the three townships (C, D, and E) showing the excessive rate, with a total population of 19,428, the mill-village population (9833) makes up 50 per cent. of the total population (excluding the city of Spartanburg), while in the remainder of the county, with a total population of 30,937, the mill-villages have a population of only 3600, or 12 per cent. of the whole. It might be supposed that a large mill-village population showing a relatively high prevalence would tend to increase the prevalence of the disease in the surrounding rural districts.

The apparent fact that cases of pellagra are excessively prevalent in the mill-villages where the population is congested, suggests the question whether the congestion of population itself may not have an important influence upon the incidence of the disease. The average density of population for the county as a whole is 109 per square mile, while for the rural districts, exclusive of Spartanburg City, it is 86.5. For the rural population, exclusive of the mill-villages, it is 60.3. In the three townships C, D, and E, which show a striking excess of pellagra among the rural population compared with the rural population of the eight other townships, the density of rural population is 72 per square mile, and in the remaining townships it is only 56, a difference in density of 16 per square mile. While the greater density of population in townships C, D, and E might be a causative factor in the greater prevalence of pellagra in the rural population of those townships, the rate of prevalence does not vary strictly as the relative density of population in each township, though it shows some tendency to do so.

Further evidence that density of population alone is not accountable for the greater prevalence of the disease in mill-villages is found within Spartanburg City itself. There the mill-villages, which are continuous with and an integral part of the city, present a rate of 142 per 10,000, whereas the remainder of the city population, living under approximately the same condition of congestion, gives only 29 per 10,000. Furthermore, the non-mill-village population within the city, with a density which is certainly over 3000 per square mile, shows almost exactly the same prevalence of pellagra per 10,000 as does the strictly rural population of the surrounding township, with only 90 inhabitants per square mile.

These figures would seem to indicate that while congestion of population may play a part in the prevalence of the disease, it alone does not explain the marked inequality of distribution between the mill-villages and the strictly rural population.

VI. RACIAL DISTRIBUTION. The distribution of the cases of pellagra in the county between the races presents a second marked inequality. While in South Carolina as a whole the number of whites and negroes is about equal, the negroes being slightly in excess, in Spartanburg County the whites predominate numerically in about the proportion of two to one, the actual figures being, whites 57,055, negroes 26,410 (Table III). The 57,055 whites gave 257 cases of pellagra, or at the rate of 45 per 10,000; the 26,410 negroes gave 25 cases of pellagra, or at the rate of 9.5 per 10,000. In other words, while whites are present in the population in the proportion of two whites to one negro, there are ten white pellagrins to one negro pellagrin.

One fact of fundamental importance in the racial comparison is the practical absence of negroes from the mill population. It follows that a more accurate comparison between the races can be made by comparing the rate of prevalence among negroes with the rate among whites, exclusive of the mill population. We have seen that the rate among the total population, exclusive of the mill-villages, was 18 per 10,000. Subtracting the negro population and the negro pellagrins we have remaining a white population, exclusive of mill-village population, of 38,522, which gave 97 cases of pellagra, or 25.2 per 10,000 against 9.5 per 10,000 among the negroes. In other words, in Spartanburg County the disease appears to be 4.7 times as prevalent among all whites as among negroes, and 2.6 times as prevalent among whites, exclusive of the cotton mill-villages.

TABLE III.—Distribution of Pellagrins among Whites and Negroes.

	Population.	Cases of pellagra.	Rate per 10,000.	Excess of whites over negroes per 10,000 of population.
All whites	57,055	257	45.0	35.5
Whites outside of mill-villages	38,522	97	25.2	15.7
Negroes	26,410	25	9.5	

The racial incidence was carefully investigated with a view to determine whether the racial variation might be due to failure to discover cases of pellagra among negroes as readily as among whites. The practising physicians throughout the county were questioned as to the comparative prevalence among the negroes in their particular section, and as to its comparative prevalence

in this race in the past. Without exception we were informed that pellagra in negroes was of comparatively infrequent occurrence. In this connection it is well to state that many of these physicians have lived and practised medicine in the same place for many years; that they are personally acquainted with practically the entire population in their particular field of work, both whites and negroes, and that they are in general thoroughly capable of correctly diagnosing the disease.

The two colored physicians in Spartanburg were closely questioned as to the occurrence of pellagra in their practice at present and in the past, and the cases cited by them are included in our statistics. Furthermore, the information furnished by them relative to the occurrence of cases in the past is in accord with these statistics. When negroes suffering with pellagra were visited a particular effort was made to secure from them information as to the occurrence of the disease in others of their own race. A number of names were secured in this way, and many negroes suspected of having the disease were visited. Many of the planters owning large plantations and having as tenants or laborers a large number of negroes were closely questioned as to the prevalence of the disease, and in some instances canvasses were made. Notwithstanding the efforts made to discover the disease in negroes, it was impossible to find more than twenty-five cases.

It is not believed that the number of cases overlooked could materially alter the relative incidence of nearly five cases in whites to one in negroes, and the racial variation is evidently a real one, though it may possibly be explained in part by the absence of negroes from the mill-village population, which, as we have seen, shows a marked excess of pellagra compared with the remainder of the white population.

TABLE IV.—Racial Distribution of Population and Racial Distribution of Pellagra with Percentages.

State.	Population statistics. ⁵				Pellagra statistics.							
	White.		Negro.		White.		Negro.		Pellagra per 10,000 of population.			
	Number.	%	Number.	%	No.	%	No.	%	W.	N.		
Virginia	1,389,809	67.4	671,096	32.6	476	76	152	24	3	2		
North Carolina	1,500,513	68.0	697,843	31.6	1744	81	407	19	12	6		
South Carolina	697,162	44.8	835,843	55.2	1129	71	471	29	16	6		
Georgia	1,431,816	54.9	1,176,987	45.1	3127	80	741	20	22	6		
Kentucky	2,027,951	88.6	261,656	11.4	442	92	39	8	2	4		
Alabama	1,228,832	57.5	908,282	42.4	1138	58	813	42	9	9		
Mississippi	786,119	43.7	1,009,487	56.6	1387	55	1156	45	18	11		
Louisiana	941,086	56.8	713,874	43.1	338	56	269	44	4	4		

⁵ Population statistics are those of the Thirteenth Census (1910). The pellagra statistics were compiled from those reported by Lavinder in reprints from Weekly Public Health Reports, No. 106.

Table No. IV is an analysis of population by race, and of the incidence of pellagra by race for eight Southern States. The pellagra statistics in this table were secured by correspondence and, as Lavinder states, are very incomplete.

In Spartanburg County there is a marked difference in racial incidence, but any suggestion that this depends upon the factor of race alone may seriously be questioned. In Table IV it may be seen that the case incidence in the two races in the States of Alabama and Louisiana shows little difference; while in South Carolina and Georgia, and to a less extent in North Carolina, there is a marked preponderance in whites. It is possible that industrial conditions in these States account largely for this variation.

VII. SEX DISTRIBUTION. The population of the county is divided practically equally between males and females, the females being only 27 in excess. The total male population of 41,719 gave 71 cases of pellagra, or at the rate of 17 per 10,000. The female population gave 211 cases, or at the rate of 50.5 per 10,000 (Table V). In other words, pellagra appears nearly three times more frequently among females than among males. Among the white population alone this proportion between males and females remains about the same, while among the negroes the relative prevalence among males and females is nearly four females to one male. This inequality between the sexes is brought out more strikingly and in greater detail if the figures are analyzed by dividing the population according to age.

TABLE V.—Distribution by Sex.

		Number in population. ⁶	Cases of pellagra.	Rate per 10,000.	Excess per 10,000 among females.
Whites:	Male	28,758	66	22.95	
	Female	28,290	191	67.5	44.5
Negroes:	Male	12,958	5	3.9	
	Female	13,452	20	14.9	11.0
Both races:	Male	41,716	71	17.0	
	Female	41,742	211	50.5	33.5
Total population		83,458 ⁶	282	33.8	

TABLE VI.—Age Distribution of Two Hundred and Eighty-two Cases.

Age.	Total population. ⁷	Cases of pellagra.	Rate per 10,000.
0 to 5	15,194	21	10.8
6 to 9	8,852	22	24.9
10 to 19	21,860	28	12.8
20 to 44	26,239	158	60.2
45+	11,161	53	47.5

⁶ Exclusive of 4 Indians, 2 Chinese, and 1 Japanese.

⁷ Exclusive of 159 persons of unknown age.

VIII. AGE DISTRIBUTION. First, considering the prevalence of pellagra according to age, without reference to sex, we find the inequalities shown in Table VI, and graphically presented in Chart 2.

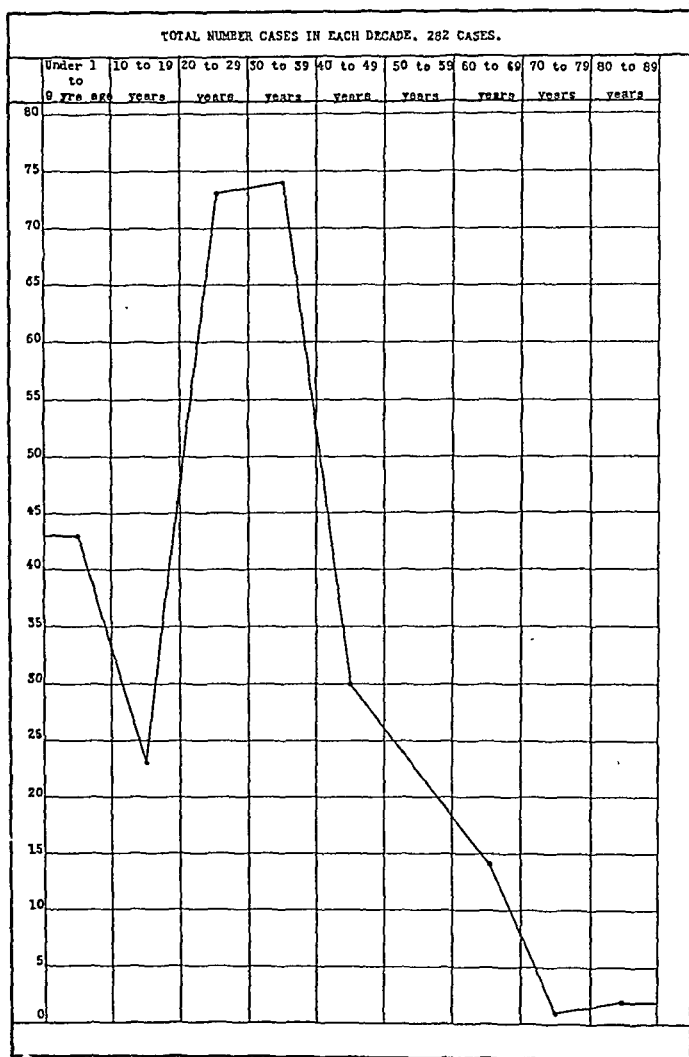


CHART 2.—Total number of cases in each decade.

In this and the following tables dealing with age distribution, in which the prevalence of pellagra is expressed in rate per 10,000 of the population, our age groups are necessarily made to conform to the age statistics for the population of Spartanburg County which could be secured from the United States Census Bureau—namely, the population of the county under six years of age, from six to nine years, ten to nineteen years, twenty to forty-four years, and forty-five years or older. The actual number of cases in these groups means little because of the wide difference in the size of the groups, both with regard to the number of years and the number

of individuals concerned. A striking excess in the rate of prevalence is apparent in the group twenty to forty-four years of age (60.2 per 10,000). The rate among those over forty-four years of age is much higher than in any other group excepting that between twenty and forty-four years. These two groups taken together, that is, the entire population over nineteen years of age compared with the entire population under twenty years of age gives the following result: Twenty years and older, 211 cases, or 56.4 per 10,000; nineteen years and younger, 71 cases, or 15.5 per 10,000.

Dividing the younger group we find that children under ten years of age gave a total of 43 cases, or 17.9 cases per 10,000; those from ten to nineteen years of age gave 28 cases, or 12.8 per 10,000. Furthermore, this higher prevalence for children under ten years is found entirely among the children between the ages of five and ten years who alone gave a rate of 24.9 per 10,000, while the younger group under five years of age gives only 10.8 per 10,000, the lowest rate found in any group.

In Chart 2 the distribution of pellagra by the number of cases in each age group is shown, dividing the cases into age decades. By comparing this chart with Table VI it is evident that the curve would be considerably modified if it expressed the rate per 10,000 of population instead of the actual number of cases in our figures. The prevalence among children under ten years would not be quite so high compared with that in other groups. The relative prevalence in groups over forty years would be higher. The two groups of from twenty to forty years would still show a striking excess over all other decades. It may be said here that the marked fall in the prevalence of pellagra in the groups ten to nineteen years appears throughout our statistics, and will come out strikingly in the consideration of the family distribution of the disease.

IX. DISTRIBUTION BY AGE AND SEX. It is important to ascertain whether the excessive prevalence of pellagra among females holds in all ages of the population, and whether the excessive prevalence found in certain age groups, notably those from twenty to forty-five years, is to be found among both males and females. Referring to Table VII it may be seen that the excess among females is not the same among all ages of the population, but is confined largely to those between the ages of twenty and forty-four years. Further, under ten years of age males and females show practically the same prevalence of pellagra. From ten to nineteen years the females show a rate a little over twice that of the males; in the large group of from twenty to forty-four years the females show a rate per 10,000 over nine times greater than the male rate. Among the population of forty-five years and over the distribution between the sexes is again nearly equal.

These cases have been further analyzed by decades, with the result as represented graphically by curves in Chart 3. These curves express actual number of cases.

TABLE VII.—Distribution by Age and Sex.

Age.	Sex.	Population.	Number of cases.	Rate per 10,000.	Excess per 10,000.
Under 5	M.	7,763	10	12.9	1.9
	F.	7,431	11	14.8	
5 to 9	M.	4,490	12	27.0	0.5
	F.	4,364	12	27.5	
10 to 19	M.	10,906	7	6.4	8.2
	F.	10,954	16	14.6	
20 to 44	M.	12,822	16	12.5	97.8
	F.	13,417	148	110.3	
Over 44	M.	5,652	25	44.2	4.8
	F.	5,509	27	49.0	

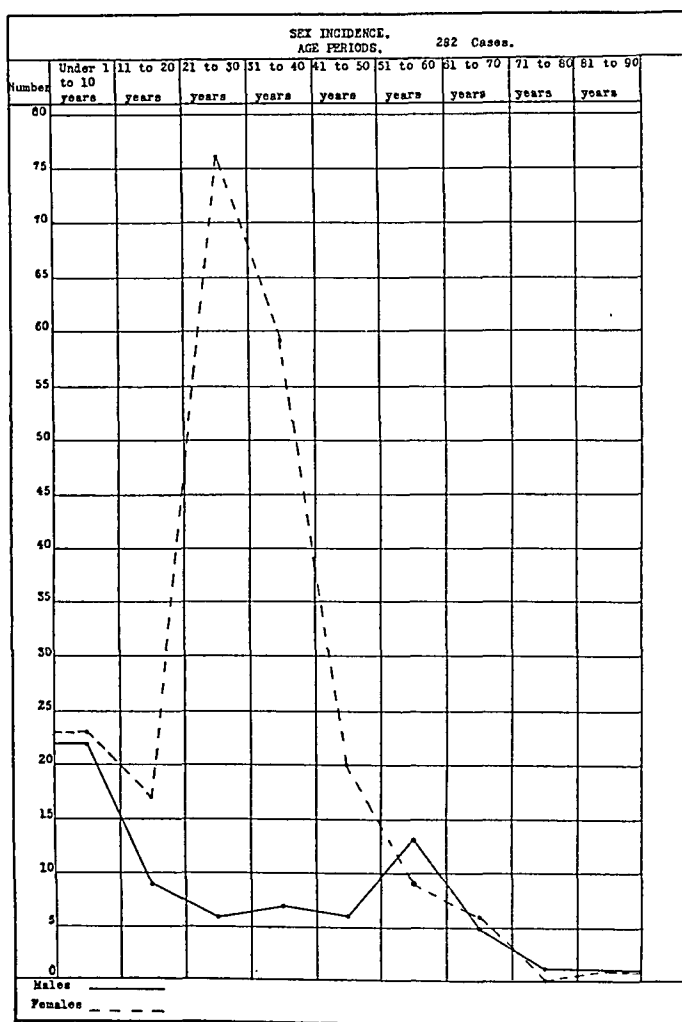


CHART 3.—Distribution by age and sex.

The fall in the curve in the second decade of life is present for both sexes, but is more marked for males: Thereafter the male curve continues to fall, whereas the female curve rises to its highest

point in the following decade (twenty-one to thirty years), drops slightly among women of thirty-one to forty years, then falls abruptly in the next decade (forty-one to fifty years) to a point somewhat below both males and females under ten years. In the decade of from fifty-one to sixty years the female curve continues to fall, and for the first time descends below the male curve, which shows a slight rise. Thereafter the number of cases is small and the two curves fall together.

The data expressed in Table VII and Chart 3 may be summarized as follows: Pellagra appears to be about equally prevalent among males and females under ten years of age and over forty-five years. Males alone show the highest prevalence in children under ten years. Females show a strikingly higher prevalence in the two decades of twenty to thirty and thirty to forty years than does either sex in any other decade.

Table VIII indicates in a general way that both whites and negroes separately show practically the same inequalities in the distribution of pellagra between the sexes in the different age groups, as has been shown in considering both races together. Any closer analysis of the figures for the two races is unsatisfactory, owing to the small number of negro cases in each age group.

TABLE VIII.—Race, Age, and Sex Incidence (Two Hundred and Eighty-two Cases).

Age.	Whites, 257 cases.		Negroes, 25 cases.	
	Male.	Female.	Male.	Female.
Under 1 to 5	9	11	1	0
Under 6 to 10	12	11	0	1
Under 11 to 20	9	14	0	3
Under 21 to 30	4	65	2	11
Under 31 to 40	6	56	1	3
Under 41 to 50	6	20	0	0
Under 51 to 60	14	9	0	0
Under 61 to 70	4	5	1	1
Under 71 to 80	1	0	0	0
Under 81 to 90	1	0	0	1
Totals	66	191	5	20

While it is not proposed to enter into any extensive comparative studies in this preliminary report, there are certain data upon the age and sex distribution of pellagra in this country which present an interesting parallel with the figures for Spartanburg County.

Chart 4 represents by curves based on actual number of cases the age and sex distribution of 164 cases of pellagra, 99 of which were reported by Mizell,⁸ of Georgia, and 65 by Tucker,⁹ of Virginia.

⁸ From paper read at the Second Triennial Meeting of the National Association for the Study of Pellagra, Columbia, S. C., October 3, 1912.

⁹ Beverley R. Tucker, M.D., A Discussion of Pellagra, with Remarks on Sixty-six Cases Occurring Outside of Institutions, *Old Dominion Jour. Med. and Surg.*, April, 1911, vol. xii, No. 4.

Chart 5 shows mortality rates for the State of Texas. This chart was furnished to us by Dr. H. K. Beall, of Fort Worth, Texas,¹⁰ who first directed attention to the inequalities of distribution by age in males and in females.

Chart 6 is based upon death reports of pellagra in Alabama between June, 1909, and December, 1912. These reports cover a total of 1148 cases during this period. The data were kindly supplied by Dr. W. H. Sanders and Dr. H. G. Perry, of the Alabama State Board of Health.¹¹

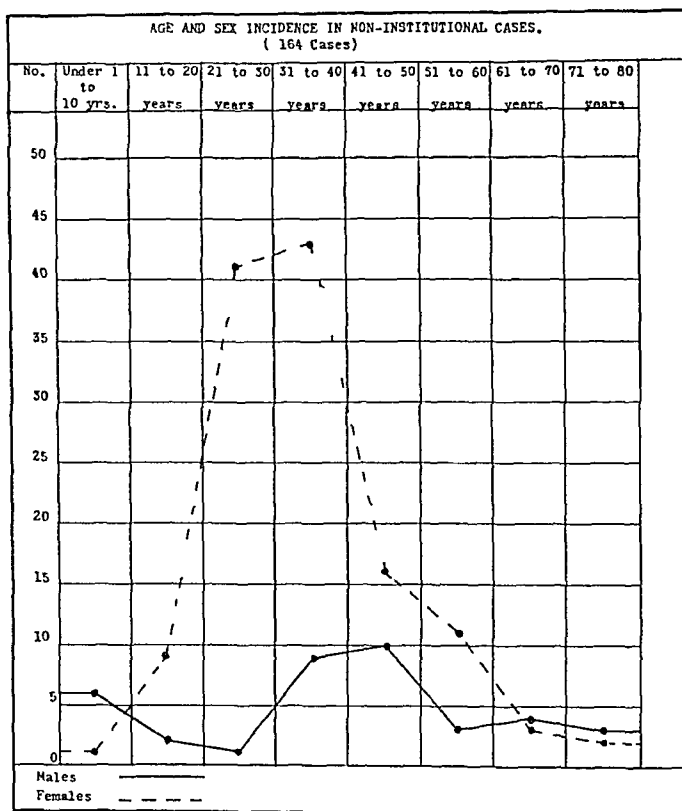


CHART 4.—Age and sex incidence in non-institutional cases.

Chart 7 presents a graphic representation of mortality rates for pellagra in the State of North Carolina for 1911 and 1912. We have to thank the health authorities of North Carolina for the information on which this chart is based.¹²

The data from these five sources are all the statistics available to us at the present time which lend themselves to a comparison with our own figures regarding age and sex distribution. It should be noted that the curves in Chart 4, like our own, are based on morbidity statistics, while Charts 5, 6, and 7 are based upon death reports.

¹⁰ Personal communication.

¹¹ Ibid.

¹² Ibid.

A comparison of the four charts shows considerable variation in both the male and the female curves in different age groups.

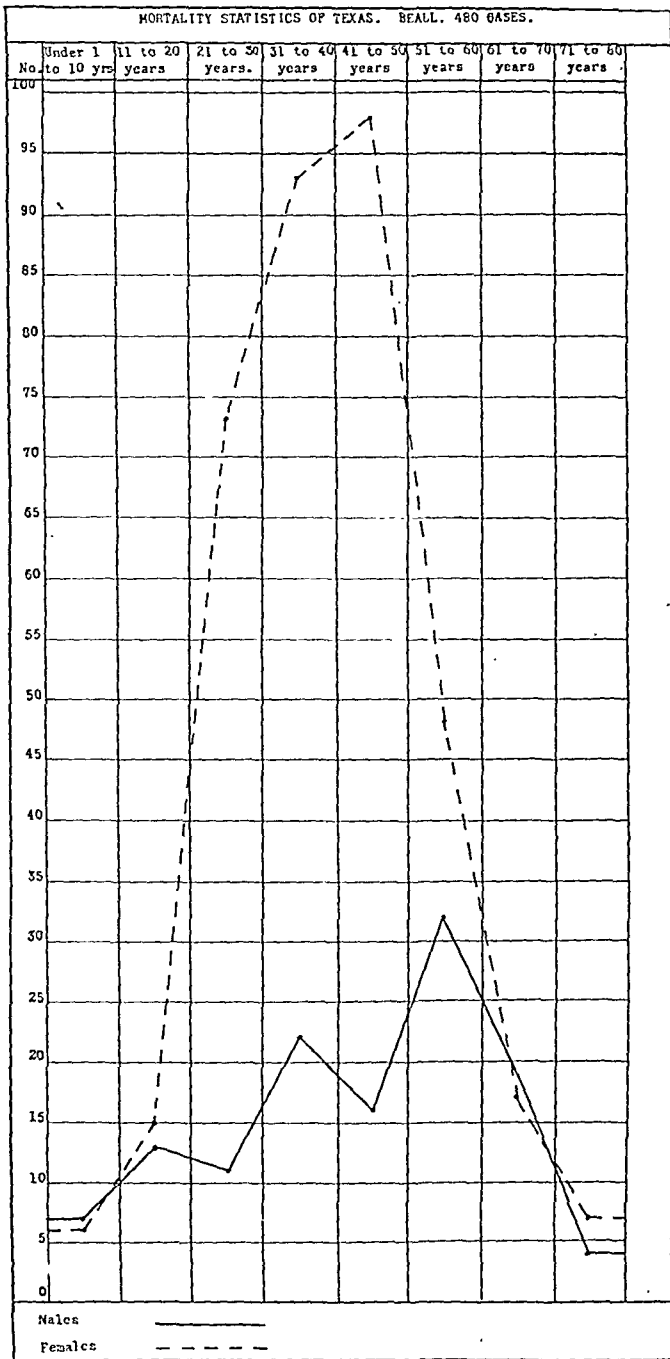


CHART 5.—Mortality statistics of Texas.

They all agree, however, in showing a strikingly excessive prevalence among females of middle age and a comparative equality

of distribution between males and females in childhood and among people of advanced age.

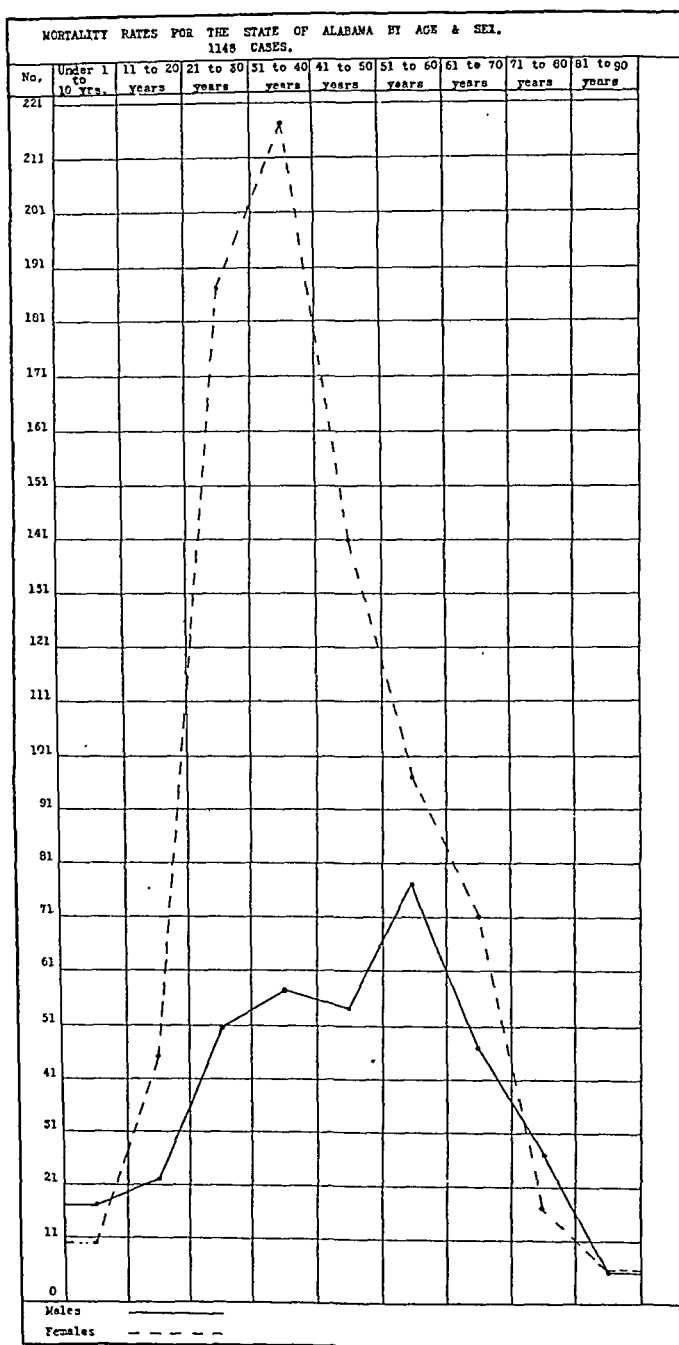


CHART 6.—Mortality rates for the State of Alabama by age and sex.

X. DISTRIBUTION BY OCCUPATION. The consideration of the relationship between occupation and the incidence of pellagra in Spartanburg County resolves itself almost entirely into a dis-

cussion of the relative prevalence of the disease among field laborers, workers in the cotton-mills, and those engaged in housework. Only a few scattered cases gave other employment. The actual data with regard to occupation obtained from 234 cases of pellagra is set forth in Table IX: 110 (47 per cent.) gave housework as their occupation exclusively; 14 others (6 per cent.) gave housework as their chief employment; 16 (6.8 per cent.) were employed in housework part of the time, working the remainder of the time in the mills; 18 (7.7 per cent.) worked alternately about the house and in the fields. Thus a total of 158 (67.5 per cent.) of

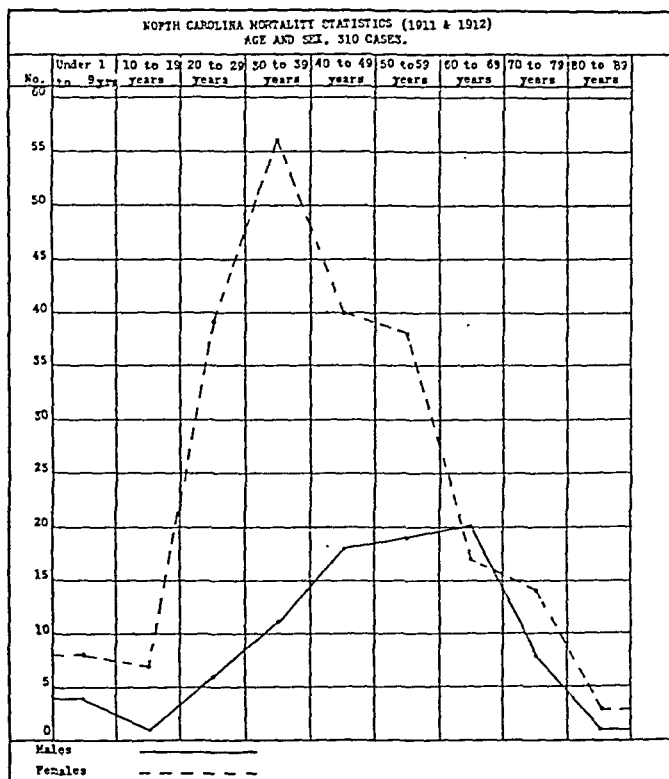


CHART 7.—North Carolina mortality statistics during 1911 and 1912.

the 234 cases, were employed in household work within the home for at least a fair portion of their time. These figures mean little more than what has already been shown by the age and sex distribution of the disease—namely, that it is excessively prevalent among adult females the great majority of whom are employed in housework. There is one further indication, however, that pellagra has a much higher prevalence among the adult females of the mill-villages who are occupied as housewives than among those who work in the mills, and this point may be more closely examined by considering the occupational distribution of pellagra in the mill population alone.

TABLE IX.—Distribution of Two Hundred and Thirty-four Cases of Pellagra by Occupations.

Occupation.	Males.	Females.	Both sexes.	Per cent. of total.
Farmers	14	..	14	6.0
Field work and housework	..	18	18	7.7
Mill work exclusively	21	20	41	17.5
Mill work, some housework	..	16	16	6.8
Housework exclusively	..	110	110	47.0
Housework chiefly, some mill work	..	14	14	6.0
Scattering ¹³	9	3	12	5.1
No occupation	2	7	9	3.8

There are available for this study 121 cases of pellagra of working age residing in mill-villages. Of these, 24 were males and 97 females; 21 (87.5 per cent.) of the 24 males were mill operatives. Of the 97 females, 12 (only 12.37 per cent.) worked in the mills exclusively; 16 additional female cases worked in the mills the greater part of the time, making a total of 28 female mill workers (or 28.86 per cent.) of the 97.

46, or very nearly half (47.42 per cent.) of the 97 women did no mill work, devoting themselves to housework exclusively; while 14 others were chiefly employed in housework, going to the mills only occasionally, making a total of 60 houseworkers, or 68.85 per cent. of the female pellagrins of working age living in the mill-villages.

We have no actual statistics regarding the proportion of males and females among mill operatives. It would seem perfectly safe to say that there are at least as many females as males, the probabilities being that they are in a considerable majority. As a rule, female operatives are preferred by the mill operators. Assuming equality between the sexes among mill workers, as may surely be done with safety, the data above presented has a highly important significance, in that it shows a nearly equal prevalence of pellagra in males and females who are employed in the mills as operatives—namely, 17 males and 12 females—if we include only those women doing mill work exclusively, and 28 females if we include the 16 who gave mill work as their chief but not exclusive occupation. This comparative equality as regards the prevalence of pellagra between the sexes among mill operatives is in striking contrast to the inequality between adult males and females in our sex statistics for the population as a whole, and is very closely in harmony with what is known of sex distribution in institutional cases where a difference in prevalence between the sexes is absent or slight.

In comparing the mill-village population with the rural popu-

¹³ Two patients were merchants, two dressmakers, one was employed in each of the following occupations: insurance, student, carpenter, butcher, clerk, railroad fireman, day laborer, school teacher.

lation as regards the prevalence of pellagra, we found the disease nearly seven times as prevalent in the mill-villages as in the rural districts, the actual rate of prevalence in the mill population being 104 per 10,000. Out of the total mill-village population of approximately 19,000, about one-half, or 9500, are actually employed in the mills. Among these mill operatives we have 57 cases of pellagra, including those patients who gave mill work as their chief but not exclusive occupation. These 57 cases give a rate of 60 per 10,000 among actual mill operatives, against 104 per 10,000 for the total mill-village population. The 41 patients giving a history of mill work exclusively present a rate of only 43.2 per 10,000. These figures seem to indicate that the excessive prevalence of pellagra in the mill-village population is not found among those who actually work in the mills, but among the women engaged in the day about the houses, and the children who are at home with them.

While children under working age do not form a part of an occupational study, it may well be noted in this connection that 30 mill-village children under ten years of age had pellagra. These cases added to the 60 adult females in the mill-villages engaged in housework exclusively make a total of 90 cases of pellagra in the mill-village population of the county, which by occupation were about the dwellings during the day, against 57 cases among the population engaged in mill work. The 57 operatives give a rate of 60 per 10,000 for the half of the mill-village population which works in the mills. The 90 houseworkers and children give a rate of 94.7 per 10,000.

XI. DISTRIBUTION OF CASES IN FAMILIES. 316 cases of pellagra are available in our data for a study of family and household relationships, and these cases represent 223 families, an average of 1.42 cases of pellagra per family. An analysis of the family distribution is given in Table X. About half the total number of cases occurred singly in families, and about one-fourth of the total number occurred two to a family. Of the total number of families with pellagra (223) nearly three-fourths (160) had but one case, and nearly one-fifth gave but two cases. Nearly one-tenth of the families gave 3, 4, or 5 cases.

In view of the inequalities found in the prevalence of pellagra in the two sexes, and at different ages, an attempt has been made to discover whether the sex and age distribution differs among cases which occur singly in families from the distribution among cases occurring two or more to a family—in other words, to determine whether cases developing singly in families are apt to be of any particular age or sex, and to differ in these respects from multiple family cases. For this purpose, 294 cases for which age and sex statistics are available have been charted (Chart 8) by age periods of five years each—cases occurring singly in families being represented by a solid line, and cases occurring two or more to

a family by a broken line. The upper two curves represent male cases alone; the middle curves, females alone; and the lower curves, the two sexes combined. The curves represent the percentage of the total 294 cases and not the actual number of cases in each group. Accordingly, the solid line and the broken line would coincide wherever the same condition of distribution exists between single cases and cases occurring two or more to the family.

TABLE X.—Distribution of Pellagra in Families.

	Number of families.	Number of cases.	Percentage of total number of families.	Percentage of total number of cases.
One case to one family . .	160	160	71.7	50.6
Two cases to one family . .	42	84	18.8	26.6
Three cases to one family . .	14	42	6.3	13.3
Four cases to one family . .	5	20	2.3	6.3
Five cases to one family . .	2	10	0.9	3.2
Total with more than one case to one family . .	63	156	28.3	49.4

The most striking inequality between the two curves is present among children under ten years of age. Not only is the curve for multiple family cases higher than the curve for single cases in both males and females, but for males alone and for the combined sexes it goes higher among children under ten years than in any other age group. In this respect it presents a striking contrast to the curve for single family cases and to our general age distribution. It is remarkable, further, that this excessive prevalence in multiple family cases is much greater among males than among females, especially in the younger group of children under six years of age. Among cases occurring singly in families the curve never goes above 5 per cent. in any age group under twenty years among males, females, or the sexes combined. These facts seem to show that where single cases of pellagra occur in families it is rarely children under ten years who are the ones attacked. Among families with more than one case, however, children under ten years form a higher percentage of the cases than does any other decade. Among families with but one case it would appear that the two decades from twenty-one to forty years give the great majority of cases among females, while among males more single cases occur among those over fifty years.

When considering the subject of age and sex distribution, attention was called to the striking fall of prevalence apparent among persons from eleven to twenty years old. Inspection of the curves in Chart 8 shows this fall to be confined almost entirely to cases which occur two or more per family, the indication being that

isolated cases in families are as apt to arise among individuals from eleven to twenty years of age as among children under eleven years.

**The Age and Sex Distribution of Pellagra in Families
with a single case and in Families with two or more cases**

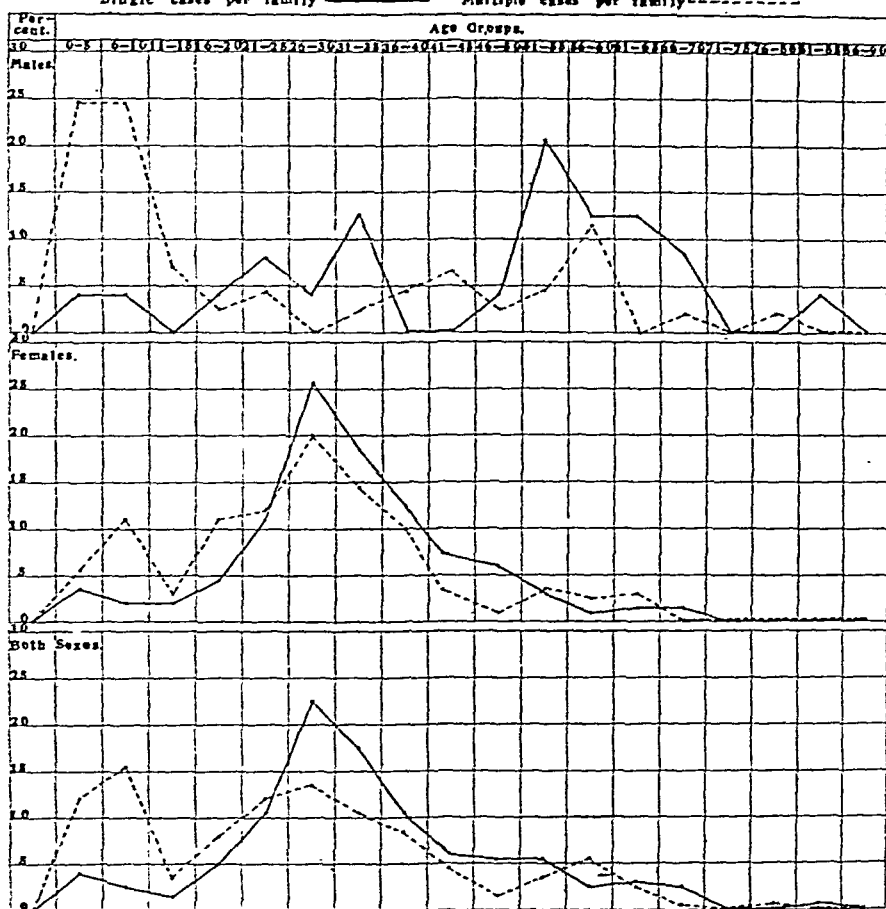


CHART 8.

It is not considered advisable to proceed farther at the present time in an analysis of the family relationships of pellagrins. Such further investigation would carry us into a study of each individual family, the actual sequence of cases in each family, and, furthermore, would introduce the whole subject of household association and its significance with regard to the family relationship. As yet our data are not sufficiently complete to make such a study in a satisfactory manner. It may be said, however, that while there is some evidence in our preliminary investigation that family relationship *per se* does seem to have some influence upon the incidence of pellagra, there are stronger indications that household association is a more important factor in the distribution of the disease.

(To be concluded.)

THE DIAGNOSIS OF INFLAMMATION IN THE ANTERIOR OCULAR SEGMENT.¹

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THE ability to diagnosticate ocular inflammations is of the utmost importance. Delay in instituting treatment may result in irreparable damage to the ocular tissues, and faulty diagnosis may be followed by treatment fatal to vision. Far too often has the sight of a glaucomatous eye been destroyed by the instillation of atropine under the impression that the disease was iritis.

The purpose of this paper is to facilitate diagnosis by calling attention to the signs indicative of the forms of inflammation likely to be encountered in one's daily work.

Inflammations in the anterior ocular segment may be divided into those of the conjunctiva, the cornea, the iris and ciliary body, glaucoma, and inflammations consecutive to violence.

These inflammations have as the most noticeable feature vascular injection. The vessels participating in this injection are either the posterior conjunctival or the anterior ciliary, and depending upon which of these systems is congested we speak of conjunctival or ciliary injection. Conjunctival injection appears as a superficial network of bright red bloodvessels whose position in the conjunctiva is demonstrated by the fact that movement of this membrane causes a corresponding change in position of these vessels. The vessels can be individually distinguished. This is the injection of conjunctivitis. Ciliary injection appears as a dark red or violaceous zone surrounding the cornea, and its position beneath the conjunctiva is demonstrated by the fact that movement of this membrane does not result in a change of position of this zone. Instead of the individual vessels being distinguishable there is a general diffuse redness. This is the characteristic injection of inflammation of the cornea and iris and ciliary body.

Acute contagious conjunctivitis, or pink eye, is the classic type of conjunctivitis. The symptoms, conjunctival injection, lachrymation, photophobia, and mucopurulent discharge together with some burning and itching of the eyes, are those which exist with slight variations in all forms of conjunctivitis. This form of conjunctivitis responds readily to argyrol and boric acid flushings, and is of interest because of its epidemic tendency, one case frequently being responsible for the spread of the disease through an entire school.

¹ Read before the staff of the Physicians' and Surgeons' Hospital, Wilmington, Delaware, October 7, 1912.

Gonorrheal conjunctivitis, of which there is the adult form and that seen in the newborn, is a destructive disease which beginning as conjunctivitis may rapidly extend to the adjacent tissues, producing in a few days even a purulent panophthalmitis. Thanks to Crede this is now a rare disease in the newborn. By the use of silver nitrate instillations in the eyes of all infants born in the Leipsic Lying-in Asylum, Crede reduced the percentage of ophthalmia neonatorum from 10.8 to between 0.1 and 0.2. The benefits obtained from this treatment are so immeasurable that Crede's prophylactic treatment cannot be too often retold. During the first bath the eyes are cleansed with pure water—not that of the bath—and cotton, and one drop of a 2 per cent. silver nitrate solution instilled into each eye. Since ophthalmia neonatorum may originate from other than gonorrheal organisms, this treatment should be used in all newborn infants. Most of the cases of gonorrheal conjunctivitis we now see belong to the adult form, and occur in patients suffering with gonorrheal urethritis or in those who have become infected through using the towels and linen previously used by gonorrheal subjects. After an incubation period varying from two or forty-eight hours the lids become red and swollen, often to such a degree that they can only with difficulty be separated. The tarsal and ocular conjunctivæ are intensely edematous, and have a rough, granular appearance. The swelling of the ocular conjunctiva ends abruptly at the margin of the cornea, and the cornea appears as if lying in a pit. The secretion during this stage is serous and tinged with blood, having much the appearance of beef juice. After two or three days the secretion becomes purulent, and the chemosis and swelling begin to subside. The most dreaded complication is involvement of the cornea, resulting in ulceration and even panophthalmitis. Treatment must first be directed toward the prevention of the infection of the second eye if it is still uninfected. This is done by hermetically sealing this eye with a watch-glass strapped down with adhesive tape. Treatment of the infected eye consists of cold compresses, instillations of argyrol, and frequent cleansing of the eyes with 1 to 5000 potassium permanganate solution. As soon as pus begins to flow from the eyes and the swelling in the lids is sufficiently reduced to allow of their eversion the tarsal conjunctiva must be painted with a 2 per cent. silver nitrate solution twice daily, care being taken that the solution does not come in contact with the cornea. When the cornea appears cloudy or its surface dulled, hot compresses must be substituted for the cold, in the effort to stimulate corneal nutrition. Gonorrheal ophthalmia is so contagious that the most rigid isolation of these patients is necessary. While it is rare to find an infection of the conjunctiva showing such violent inflammation as that seen following a gonococcal invasion, other organisms will sometimes give rise to a condition which in the early stages resembles

gonorrheal conjunctivitis. A resort to microscopic examination will differentiate these conditions, as the gonococcus is present if the inflammation is due to its influence.

In scrofulous children, phlyctenular conjunctivitis is a common disorder. This disease shows, in addition to the usual signs of conjunctivitis, small reddish tumefactions, about the size of a split pea or smaller, around the margin of the cornea, and often in the cornea itself. After two or three days these phlyctenules break down into small ulcers, which rapidly heal over, only to be succeeded by new crops, the process continuing over weeks and months. If, in the cornea, they leave after healing permanent opacities, which when central materially interfere with vision. Treatment of phlyctenular conjunctivitis, or if the cornea is involved, phlyctenular keratitis, should aim toward the upbuilding of the general system. The local treatment consists of atropine for its sedative effect, frequent cleansing of the eyes, and protection of the eye from light by the use of dark glasses.

Inflammation of the cornea, keratitis, shows in addition to ciliary injection some change in the polish and evenness of the surface, or some loss in the transparency of the cornea. Superficial lesions of the cornea, for example, a phlyctenular or other ulcer, appear as spots in which the lustre and evenness of the cornea are lost, the area being somewhat depressed below the general surface. If fluorescein is dropped into such an eye the spots stain a bright green. A whitish halo of corneal infiltration surrounds each of these areas. Change in the transparency of the cornea is due to change in the deeper layers, such, for example, as is seen in interstitial keratitis. Were one to examine the eyes of the little victim of congenital syphilis, with his large forehead, deeply lined face, and weeping eyes, gray or whitish spots deeply situated in the generally cloudy cornea could be seen; or if these spots were so numerous as to have become confluent, the cornea would have a general ground-glass appearance, often so dense as to obscure the underlying iris. Closer examination of these eyes would show vascular twigs, branching broom-like, appearing suddenly from beneath the corneal limbus, and penetrating toward the pupillary area.

In iritis and inflammation of the ciliary body, cyclitis, the characteristic changes are naturally in these tissues, and, owing to their location, changes occur also in the aqueous and anterior chamber. The iris is hyperemic and swollen, and as a result the pupil is small and non-responsive to light. Inflammatory exudates in the iris tissue result in change of color of the iris, readily observed by comparison with its fellow iris. The aqueous is turbid, and frequently deposits are seen on the posterior surface of the cornea as small dark-colored points over the lower half of Descemet's membrane. The pupillary margin of the iris, where it lies in con-

tact with the anterior lens capsule, becomes glued to this structure at various points. These points of attachment, posterior synechia, upon dilatation of the pupil with atropin, become evident, as a result of which the pupil appears irregularly round, the attached points not yielding to the drug action. Aside from traumatism, iritis generally arises as a result of some constitutional condition, of which syphilis and rheumatism are the most frequent. Tuberculosis, gonorrhea, metabolic disturbances, and acute infectious fevers are responsible for a certain proportion of the cases. Treatment must therefore be directed against the constitutional condition. Locally, antiphlogistic measures and atropine should be employed. Potassium iodide and mercury facilitate absorption of the inflammatory exudates.

When there is a disproportion between the inflow and outflow of the circulating fluids in the eye, the inflow being in excess, there is a rise in intra-ocular tension. Such a condition is called glaucoma. The symptoms of glaucoma, including cupping of the nerve head and loss of sight, originate as a consequence of this elevation of tension.

Beginning with gradual elevation of tension, lasting over months, during which time the patient has attacks of cloudy vision, dull headache, sees colored rings around the street lights (halo vision), the attacks becoming more frequent and severe with the progress of the disease, this prodromal stage finally culminates in an acute glaucomatous attack, with violent pain in the eye, face, and jaws, vomiting and fever, sudden and almost complete loss of vision, injection of the eye, and a dilatation and rigidity of the pupil. The tension at this time, if tested, would be found to be extremely high. With these symptoms the trouble can be easily recognized, yet these attacks are sometimes mistaken for hemicrania. Such an attack may result in blindness in a few hours or, as more usually happens, the tension gradually goes down and the irritating signs disappear, leaving as a permanent aftermath slight reduction in visual acuity. A few weeks later, with a gradual elevation of the tension, a second attack supervenes, only to be succeeded by future attacks, each of which leaves the eye more permanently impaired, until finally it is stony hard, totally blind, and the seat of constant severe pain. This so-called acute inflammatory glaucoma is a rare condition.

In chronic inflammatory glaucoma, the more usual form, the eye passes gradually from the prodromal stage into a glaucomatous condition, with increasing redness of the globe, increasing dilatation of the pupil, and the iris slowly becoming atrophic. The tension rises slowly, but persistently, and at the same time the visual acuity recedes. The attack is not so severe as occurs in acute glaucoma, although the ultimate result of the disease is the same in both forms. Chronic inflammatory glaucoma is sometimes mistaken

for iritis, and unfortunately treated with atropine. One of my preceptors in ophthalmology not long ago told me of the following experience. A medical practitioner brought a patient to him who for the previous three weeks had been using, with no apparent benefit, medicines prescribed for conjunctivitis. The inflammation happened to be iritis, and promptly subsided under proper treatment. The mental process at work in the mind of this practitioner must have been as follows: if a case when treated as conjunctivitis does not get well, try atropine, it may be iritis; for not long after he called in the same consultant to ascertain why, in another case, atropine was not yielding the desired result. This case was, unfortunately, chronic inflammatory glaucoma, and when first seen by the oculist the sight was entirely obliterated. I have encountered three cases of a similar nature, in each of which the sight was lost.

The uveal tract (iris, cilia y body, and choroid) supplies the ocular fluids, and Schlemm's canal is the channel through which the excess is carried off. In order to reach Schlemm's canal these fluids must first filter through the ligamentum pectinatum, a layer of loose cellular tissue which extends from the root of the iris forward to the point of junction of the sclera and cornea in the filtration angle. Dilatation of the pupil allows the iris to fill in this angle and overlies the ligamentum pectinatum, thus impeding the outflow of the ocular fluids. This happens in glaucoma, and if in such a condition further dilatation of the pupil is induced, as by the instillation of atropine, the filtration of the ocular fluids is further impeded.

Still a third form of glaucoma, chronic non-inflammatory, has, as can be inferred from its name, little or no inflammatory reaction, the diagnosis depending upon the ophthalmoscopic findings and the behavior of the visual fields.

The types of glaucoma above described are classified as primary in contradistinction to secondary glaucoma, in which either during or as the result of some other ocular disease the intra-ocular tension rises above the normal. Secondary glaucoma is sometimes observed in the treatment of iritis, where, as a result of the dilatation of the pupil, the iris is pushed into the filtration angle, thus interfering with the outflow of the ocular fluids. After a severe iridocyclitis, with the production of a total annular synechia, or a pupillary membrane, the posterior chamber is completely closed from the anterior, in this way blocking the natural lymph flow.

Violence to the eye may result in inflammation to one or more of the ocular tissues, and will show the type of inflammation characteristic to the tissues involved. Traumatism may result in a rupture of the ocular tunics, with or without coincident prolapse of the contents of the eye. Stab wounds and the penetration of foreign bodies also causing breaks in the ocular tunics; all such injuries

bring up the question of a retained foreign body, and where the history of the accident does not settle this point, efforts should be made to locate a foreign body by means of direct, ophthalmoscopic, and x-ray examinations. If located, efforts must be made to remove the foreign body. The character of inflammation generally set up as a result of penetrating wounds of the globe and retained foreign bodies is iridocyclitis. Iridocyclitis of traumatic origin is responsible for the majority of cases of sympathetic inflammation in the second eye. Patients suffering from an iridocyclitis of the above-mentioned character must therefore be carefully watched for the beginning signs of sympathetic inflammation, which are photophobia, lacrymation, ciliary injection, deposits on the posterior corneal surface, posterior synechia, vitreous opacities, and hyperemia of the retina and optic nerve head. With the development of these signs in the uninjured eye removal of the injured eye is imperative.

The subjective symptoms of the inflammatory diseases in the anterior ocular segment yield little definite information except in glaucoma.

It is seldom that one of the ocular structures is the seat of disease without some involvement in the adjacent tissues. And so involved may this participation of two or more tissues in one inflammatory process become that even the skilled oculist has difficulty in properly differentiating the existing signs. Conjunctival injection denotes conjunctivitis, and ciliary injection shows the process to be of deeper origin. Ciliary injection occurring in the course of conjunctivitis shows an extension of the inflammation to the deeper tissues. Conjunctival injection often exists simultaneously with ciliary injection in severe inflammations, but in these cases the significant sign is the ciliary injection, and it is incumbent upon the physician to ascertain the cause for its presence, and not regard the case as merely a conjunctival inflammation. In iritis the pupil is contracted, whereas in glaucoma it is dilated. In conclusion, let me once again warn against the instillation of atropine or other mydriatic into an inflamed eye until the possibility of glaucoma as a cause of the symptoms is eliminated.

EPIDIDYMITIS DUE TO THE COLON BACILLUS.

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THE subject of colon bacillus infection of the urinary tract has for some time been receiving considerable attention, and as a result cases have been reported where this group of organisms

was found in pure culture accompanying pathological conditions in all these structures. It has also been shown that they may be frequently found in the urine where no pathological condition is present. The frequency, therefore, with which these organisms may be found present under both normal and abnormal conditions leads one to believe that possibly they may be the cause of disturbances in these organs much more frequently than has been supposed. Aside from cystitis, where for some time it has been known that the inflammation, in the majority of instances, was due to the colon bacillus, these organisms did not appear to play an important role in diseases of the urinary organs, though there would seem to be no reason why other organs should not be equally liable to involvement under similar conditions. I have felt satisfied for some time that cases of chronic gonorrheal urethritis were prolonged by the presence of these organisms, and while they have not seemed to be especially virulent in these cases, it is often difficult to get rid of them; but when this is accomplished, I have found that the chronic urethritis improved.

I was lately asked by a friend to examine some slides of secretion from the genital organs of a woman who complained of a discharge which stained her underclothes and who was found to have a Bartholinitis. There was a great profusion of colon bacilli, but no other organism could be found. Her husband had probably not been infected, as he made no complaint. I have at present under treatment a young man who one week after intercourse noticed a slight discharge from the urethra unaccompanied by any marked urinary symptoms, except some slight increase in frequency of urination, and where the only organism to be found in the discharge was a profusion of those resembling colon bacilli. Massage of the prostate showed the same organisms in the expressed fluid. Naturally the question arising in this case is whether he has acquired the infection in intercourse or was the infection derived from his own system?

While it seems reasonably certain that these organisms, though perhaps under ordinary circumstances they are not very virulent, may quite frequently be the cause of inflammatory conditions of the urinary tract, still there are few cases recorded of epididymitis as a result of colon bacillus infection, a complication of frequent occurrence in other infections, such as gonorrhea and tuberculosis.

The manner in which infection of the urinary tract is brought about is still a matter of discussion, and it is also unsettled as to whether it is necessary that a lesion of the intestinal tract be present before the organisms are liberated. In epididymitis occurring with some other diseases we see cases where it seems clear that the epididymis becomes involved by direct extension through the ejaculatory ducts from the posterior urethra or from the prostate. Whether it would be possible for infection to take place in this

way, supposing no inflammatory lesion to be present about the opening of these ducts, is questionable, though we find reports of cases of epididymitis where colon bacilli were found in the urine, but no symptoms of urethritis were present. In such cases the possibility of infection taking place in such manner must, of course, be considered. It is to be remembered, however, that a mild posterior urethritis or proctitis may give rise to no marked symptoms, and it might be possible in some cases to overlook it unless a careful examination was made.

Dr. George G. Smith¹ reports a case of epididymitis following typhoid fever where colon bacilli were found in the urine and culture of the fluid from the epididymis after operation showed pure culture of typhoid bacilli. Epididymitis following typhoid fever is a complication somewhat rarely seen, and the majority of works do not mention it at all. There is considerable doubt as to whether it is an orchitis or epididymitis. Both Osler and Pepper speak of it as an orchitis, and Osler says, it occurs with a mild catarrhal urethritis. In Sajous' *Annual* there is no mention of orchitis or epididymitis in the article on typhoid fever. It does, however, state that "Pus is not infrequently found in the urine of typhoid patients," and says, "It may arise from cystitis or pyelitis." In the same article, under pathological anatomy, we find: "Catarrh of the bladder is sometimes met with, and may be brought about by the careless use of the catheter for retention." So it would seem that uncertainty exists not only as to whether it is an epididymitis or an orchitis, but as to the effect of the typhoid bacilli on the urinary tract as well. It is unfortunate that so many loose statements are made in medical works that it is often difficult to get at the real facts. In Smith's case the operation showed that it was the epididymis which was affected, and the testicle was only slightly if at all involved.

The condition of the intestinal tract in these cases might, with little doubt, afford an open gateway for the escape of the organisms into the circulation, and unless it can be shown that a posterior urethritis is present it would seem more reasonable to suppose that infection takes place in that way notwithstanding the fact that the organisms may be found in the urine, rather than to believe that they pass into the epididymis through the openings of the ejaculatory ducts. Generally speaking, an epididymitis seems to be preceded by a posterior urethritis or proctitis, while orchitis results from blood infection.

In inflammation of the testicle following mumps the infection is undoubtedly carried by the blood stream. Nothing is known as to the nature of the infection, as these cases seldom come to autopsy, and are never operated upon. In like manner in syphilis the testicle is the part first involved.

¹ Trans. Amer. Urolog. Assoc., 1912.

It is of interest to observe that since operations for gonorrheal epididymitis have become more frequent, cultivation of the fluid obtained from the inflamed part, while frequently showing the gonococcus on cultivation, in some instances no organisms can be found. It is assumed, however, that the gonococcus is the cause of the inflammation, since it follows a gonorrheal urethritis. Hagner in several articles on the subject has an interesting series of cases showing the results of such examinations after operations.

In tuberculosis it is the epididymis which nearly always is involved before the testicle becomes affected. But in tuberculosis it is believed by many that the epididymis is always a secondary involvement to tuberculosis elsewhere, and is frequently dependent on tuberculosis of some of the urinary organs.

CASE.—J. D. I., an unmarried man, aged thirty-seven years, was referred to me on May 7, 1912. The previous day he had begun to have frequency of urination accompanied by much pain and tenesmus. The only cause which could be assigned for the trouble was that he had partaken freely of asparagus for dinner the night before, and had also had a cocktail or two. He never had urethritis, but had been treated for catarrhal prostatitis some two years before, which had been relieved by massage and instillations of silver nitrate, otherwise he had been perfectly well.

Examination showed no inflammatory condition of the meatus or urethra, and no discharge was present. Urine passed in two glasses was equally cloudy—in both the cloudiness was due to pus. The urine was not high colored, as he had begun to drink water freely as soon as the frequency of urination had commenced. Examination of the prostate did not reveal any marked prostatic trouble. His tongue was heavily coated, but there was no apparent intestinal disturbance. A diagnosis of cystitis was made, and he was ordered active catharsis, hot rectal irrigations, suppositories of morphine at night, and an alkaline diuretic. After a few days of this treatment the pain, tenesmus, and frequency of urination had so much subsided that he was given bladder irrigations of a solution of boric acid.

A specimen of urine obtained from the bladder after washing with the boric acid solution was examined by Dr. Peter Irving, and showed "many pus cells, epithelium in fair amount, which looks like that from the kidney pelvis, and organisms, probably colon bacilli." A culture was made by Dr. D. S. Jessup, which proved them to be unquestionably colon bacilli. On this finding he was requested to prepare a vaccine which could be used if necessary. Dr. Irving reported the urine to contain no indican or indol-acetic acid, although a pure culture of colon bacilli was present.

On the tenth day after I first saw him he began to have some pain and tenderness in the left cord and epididymis, with some return of the urinary symptoms. Cold lead and opium solution

with an ice-bag and support for the testicle did not prevent the epididymis from becoming much enlarged and tender. He had been running an irregular temperature from the time his cystitis began. It varied from 99° to 101° , and was not markedly changed by the development of the epididymitis. The temperature did not return to normal until June 6, a period of about one month.

The first blood count by Dr. Irving, on May 11, was as follows: White blood cells, 8000; differential polynuclears, 76.2 per cent.; lymphocytes, 20.4 per cent.; eosinophiles, 3.2 per cent.; basophiles, 0.1 per cent.

During the first week of the epididymitis he was much more uncomfortable from the acuteness of the inflammation than patients ordinarily are with a gonorrhœal epididymitis. For a short time hot applications were used in place of the cold lead and opium, but were discontinued, as they did not control the pain as well as the ice. On May 23, he had a severe chill, lasting for some time, but not followed by any marked rise of temperature. Pain in the epididymis was severe if the ice was discontinued. Dr. Charles H. Peck was asked to see him, but could find nothing in the kidney or epididymis which would seem to call for operative interference. At this time the blood examined by Dr. Irving showed: White blood cells, 22,000; polynuclears, 87 per cent. There was no sign of any change taking place in the epididymis; it was large and tender, but there were no signs of suppuration. It was decided to use the vaccines which Dr. Jessup had prepared, and 5,000,000 were given in the afternoon of May 24. This was followed shortly by a chill and rise of temperature to 102.8° . Next morning there was another chill, and the temperature rose to 103° . Six days later another injection of 5,000,000 was given, and this time was followed by no reaction. Again on June 5, 10,000,000 were given without causing any disturbance. Later 30,000,000 were given, and only caused a slight reaction.

The exudation into the epididymis was extremely slow in being absorbed, and it was a considerable time before it returned to normal. Soon massage of the prostate and irrigations were begun. The colon bacilli could be found in the fluid obtained after massage for some time afterward, although the urine was perfectly clear, and they seemingly caused no disturbance by their presence.

In this case the epididymitis was due to the colon bacilli, which were found in pure culture in the urine obtained by catheter, and also found in the fluid from the prostate. The examination by Dr. Irving points to a pyelitis as well as the cystitis, which he quite evidently had. In his case there was no question as to the virulency of the inflammation in the epididymis, as I have never seen a gonorrhœal epididymitis which was any more severe, and seldom one which was so prolonged as was this one. The use of

the vaccines did not seem to me to be of any special benefit. Possibly if they had been used at an earlier stage the benefit might have been more marked. As an autogenous vaccine was used there could have been no question as to the proper strain.

The persistence of the infection is to be noticed in this case. As the organisms were found in the urine which had not been allowed to remain in the bladder, it would seem a reasonable assumption that they were passing downward from the kidney, and that for some reason, possibly due to the asparagus, they had given rise to the cystitis, with subsequent involvement of the prostate, as shown by the conditions of the gland on examination and the presence of pus and colon bacilli in the massaged fluid. As a result of the prostatitis and posterior urethritis the inflammation extended by continuity and epididymitis resulted. As I review the case it seems fair to conclude that there had not been a sudden invasion of the bacilli, but that in all probability they had been present for some time in the urine without causing any disturbance; but when suitable conditions were present, they were able to set up an inflammation which extended to the structures involved.

THE RATIONAL TREATMENT OF TETANUS, WITH A REPORT OF TWENTY-THREE CASES FROM THE EPISCOPAL HOSPITAL, PHILADELPHIA.⁹

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(Concluded from page 819, June, 1913.)

TREATMENT OF TETANUS.

A. The first logical step in the treatment of this disease is the *removal of the source which supplies the toxin*—that is, of the tetanus bacilli. If the point of inoculation is known, it should be attacked directly. The wound should be opened widely, and should be mechanically cleansed of foreign bodies and sloughs. Then it should be swabbed out with a 3 per cent. alcoholic solution of iodine, rinsed with hydrogen peroxide, and filled loosely with gauze soaked in the iodine solution. We believe all caustics should be avoided, as favoring the growth of tetanus bacilli by the formation of sloughs. If the nature of the case demands it for other

⁹ Read at a meeting of the Episcopal Hospital Clinical Society, November 18, 1912.

reasons, amputation should be done; then the stump should be left open, and treated as the original wound. Probably in many cases it will be well to follow Porter and Richardson's suggestion to excise the related lymph nodes, particularly if they are palpably enlarged.

B. The next indication is to *head off and neutralize the toxin already formed*. This involves a discussion of the THERAPEUTIC USE OF ANTITOXIN (see this JOURNAL for June, 1913, footnote on p. 814).

Before the introduction of antitoxin as a therapeutic measure the mortality was from 80 to 90 per cent. (Rose, 1897). Collective statistics of cases treated with antitoxin (1897 to 1903), according to Sawamura, showed a death rate of from 28 to 45 per cent. Of course, a collection of isolated case reports is apt to give too low a mortality, owing to the fact that surgeons who have had successful cases will report them, while the larger number do not report their unsuccessful cases. But the fact that no better results were reported from the therapeutic use of antitoxin in tetanus, in view of the remarkable successes from the use of diphtheria antitoxin, was explained on the theory that the antitoxin had not been used early enough. In 1902, Ullrich, according to Sawamura, remedied this apparent defect by collecting 13 cases in which antitoxin had been used early; but only one of these patients recovered; and of 54 collected cases, in which it was used early (subcutaneously), between 1899 and 1905, Busch (Sawamura) found the mortality was 66.5 per cent. In the elaborate statistics collected by Jacobson and Pease the mortality in 191 cases in which antitoxin was used, was 69.6 per cent.; these statistics are especially valuable because they represent series of consecutive cases from various sources. Fricker has published statistics of 40 consecutive cases: in the first 18 (1889 to 1897), no antitoxin was used, and 16 deaths occurred (88.8 per cent.); in the last 22 cases (1897 to 1902), antitoxin was used, and the mortality was only 55.5 per cent. In spite of this decrease in mortality, many physicians have denied that antitoxin has any therapeutic value in acute severe cases.

Huber has reported recently in great detail 69 cases of tetanus treated in Sauerbruch's clinic at Zurich, between 1881 and 1911. Of this whole number, 18 patients recovered and 51 died, a mortality of 74 per cent. Before 1900 antitoxin was not used, and of 31 patients treated without it, 20 died, a mortality of 64.5 per cent. Antitoxin was used in all of the 38 patients treated since 1900, but of these only 7 recovered, while 31 died, a mortality of 81.5 per cent. Huber thinks all of these 7 patients would have recovered even if no antitoxin had been given. But the total amounts used were small (the greatest amount used in any one case was 150 c.c. = 375—750 A. E.), and the mode of administration is open to criticism; this will be discussed later (p. 86).

But here, again, as in the question of its prophylactic use, we must inquire as to the frequency, the quantity, and the site of the injections. In most of the isolated case reports the antitoxin has been injected only once or twice, in small quantities, and subcutaneously.

Exactly how the antitoxin acts upon the toxin is not known. According to Solieri, the idea that its neutralizing action is a direct chemical one, as that of an acid on an alkali, has been abandoned. Dönitz taught that it could not only neutralize the toxin circulating in the blood, but also could loosen toxin already bound in the central nervous system and drive it out of its almost impregnable fortress. According to Metschnikoff, tetanus antitoxin stimulates phagocytosis. From numerous experiments Kraus and Amiradzibi conclude that antitoxin cures by drawing the toxin out of the cells where it is lodged, but does not itself enter into the toxin-containing cells. Recovery under the use of antitoxin they think depends on the possibility of this diffusion; and as such diffusion can take place experimentally through a membrane of collodion and through reeds (Schilfröhren), they think it is not necessary in the human body for antitoxin to be in direct contact with toxin for it to exert its neutralizing influence on the latter.

I. SITE OF INJECTION OF ANTITOXIN. The following sites of injection have been advocated: Subcutaneous, intravenous, intraspinal, intraneural, intracerebral, and intramuscular.

1. *Subcutaneous Injections.* This is the method usually employed, but, as already noted, the reports are not encouraging. If administered in this way, the antitoxin is absorbed by the lymphatics, transported to the veins, passes through the lungs, and finally, is distributed through the arterial system to all parts of the body. Only a homeopathic dose ultimately reaches the motor nerves through which the toxin is being carried to the spinal cord, while by far the greater part of the antitoxin is distributed to the viscera, where it can be of no possible use. Administered in this way, overwhelming amounts are required to produce any effect, and it is evidently the height of extravagance so to employ it.

The manufacturers of antitoxin recommend the administration of from 15,000 to 18,000 units (subcutaneously) every three hours; and such an amount (120,000 to 144,000 units) in the course of twenty-four hours is not unreasonable when it is recollected that only a very small fraction of what is administered subcutaneously can be expected to reach the seat of disease, while the rest is a shocking waste of a valuable and very costly remedy. For the amount mentioned (144,000 units) the cost is about \$100, even with the discount allowed to hospitals. (One dozen tubes of 1500 units each (18,000 units) cost the Episcopal Hospital, \$12.67; eight doses of 18,000 units cost \$101.56). Note the history of

Case 23, of our series; here antitoxin was administered subcutaneously in appropriate doses (99,000 units on the first day; 65,000 units on the second day; 60,000 units on the third day)—to a total amount of 224,000 units,¹⁰ and recovery followed. The cost to the Hospital, with discounts deducted, was about \$180. The patient was a very poor man, a charity case; but when told of the expense of his treatment, he and his friends collected \$10 and donated that sum to the hospital, as a "Widow's Mite."

Compare with this history the case of a severer case of tetanus (Case 11 of our series): On the first day 3000 units were administered intraspinaly; on the second day, 750 units were injected into the sciatic nerve, and 750 units deeply into the tissues around the wound. The patient recovered, and the total cost to the hospital was about \$3.

The quantities of antitoxin used in each case were logically correct, but only in Case 11 was the mode of administration rational.

2. *Intravenous Injections.* The effects of intravenous injections of antitoxin have been studied experimentally by v. Graff, both as regards prophylactic and therapeutic use:

(a) In a first series of experiments he administered the toxin by *intramuscular* injection. (a) Antitoxin was administered to 14 rabbits *before* toxin was injected; of these animals only 4 died, and not one had positive signs of tetanus. (b) Antitoxin (intravenously) and toxin (intramuscularly) were administered *simultaneously* to 8 rabbits; 4 of these died, but only 1 presented symptoms of tetanus. (c) Toxin was administered intramuscularly to 8 rabbits, and *from fifteen to eighteen hours later* antitoxin was injected intravenously; 4 of these rabbits died, 2 with only local tetanus, and 2 with general tetanus.

(b) In a second series of experiments he administered the toxin by *intranural* injection. (a) Toxin was injected intraneurally in 6 rabbits; all died of tetanus in from thirty-six hours to five days. (b) Antitoxin was administered intravenously to 19 rabbits *from six to ten hours before* a lethal dose of toxin was injected intraneurally. Only 2 of the animals lived and 17 died after intervals of from five to twenty-five days; but in the fatal cases death was attributed to intercurrent gastro-enteritis, no evidence of tetanus having been present. (c) Antitoxin was injected intravenously *twenty-four hours before* toxin was injected intraneurally; of 5 rabbits so treated none developed tetanus, 2 lived, and 3 died from

¹⁰ The nearest approach to this total quantity that we can find reported was administered to a patient under the care of Beates and Thomas. The most given on any one day was 97,940 units, the total amount being 213,700 units; but as the patient was a boy of fourteen years (weight 130 pounds), this amount may be relatively greater. Neary administered 280,000 units to his patient, who recovered; but as this quantity was spread out over a period of two weeks (10,000 units every twelve hours), it is not comparable to the doses above mentioned.

no apparent cause in from four to nine days. (d) Antitoxin (intravenously) and toxin (intraneurally) were injected *simultaneously*; of 5 rabbits so treated none developed symptoms of tetanus, yet all but 1 died in less than eight days. (e) Toxin was injected intraneurally, and *from fourteen to eighteen hours later* antitoxin was injected intravenously; of 3 rabbits so treated, the first developed local tetanus, but recovered, only to die on the ninth day of purulent peritonitis; the second developed local tetanus but recovered; the third developed local tetanus and then general tetanus, and died on the fifth day of general tetanus in spite of intravenous injections of antitoxin repeated every day. (f) Toxin was injected intraneurally, and *from fifteen to seventeen hours later* antitoxin was administered intravenously; of 7 rabbits so treated, 4 died as if no antitoxin had been given; in 1 life was prolonged by the treatment until the sixth day, when death from general tetanus occurred; and in 2 recovery ensued, although very severe general tetanus had already developed. These 2 recoveries, v. Graff thinks, are to be explained only on the ground that the antitoxin was able to neutralize toxin already absorbed by the nervous system.

The conclusion of v. Graff is that intravenous administration is the most effective method, but that subdural (intraspinal) administration holds next rank, because he believes in this way antitoxin is rapidly discharged from the cerebrospinal fluid into the blood.¹¹ Intraneural injections of antitoxin were not employed by v. Graff, but the results of Sawamura's experiments, detailed below (p. 84), as to the relative therapeutic value of intravenous and intraneural administration of antitoxin, seem to demonstrate conclusively the superiority of the intraneural method. From these experiments, to be discussed presently, it is evident that antitoxin administered only by the intravenous method is not very effective; and the same objections as to extravagance apply to this as to the subcutaneous method, only in less degree, because the antitoxin reaches the circulating toxin in shorter time, and can exert its influence sooner on the toxin already absorbed by the peripheral nerves or the spinal cord, if only it is used in sufficient quantities.

That the amount required to produce any therapeutic effect is immense, is proved by the observations of v. Leyden; he neutralized all the toxin in the patient's circulating blood, rendering it harmless to experimental animals; but his patient died of tetanus. And in a patient under the care of Blumenthal and v. Leyden, they succeeded in neutralizing almost entirely the circulating toxin, but much toxin remained in the cerebrospinal fluid. More recent observations tend to show that the amount of toxin circulating in the blood rapidly diminishes after the first few days of the disease, while that in the nervous tissues steadily increases.

¹¹ v. Graff says that L. Simon has treated 6 consecutive cases of tetanus by intravenous injections of antitoxin, with 4 recoveries.

The following advantages of intravenous administration are pointed out by v. Graff:

- (i) The antitoxin gets into the blood as soon as possible.
- (ii) This method can be used even when the point of inoculation is doubtful, or unknown, or inaccessible. He recommends it especially for cases of puerperal origin.
- (iii) It is easier than intraspinal or intraneural injection, is less painful, and can be repeated.

As regards the first advantage, it may be replied that it is more important to have the antitoxin in the nerves and spinal cord than in the blood. Intravenous administration is not the only available method for cases mentioned in the second paragraph, since intraspinal (subdural) injections may be made; and these, as well as intraneural injections can be repeated as often as is desirable. However, they are more painful to the patient, sometimes requiring a general anesthetic, and intraneural injections require more accurate anatomical knowledge and surgical skill.

3. *Intraspinal (Subdural) Injections.* These were originally suggested by Jacob; but he came to the conclusion, after some experimental work, that they were useless, because he thought all the antitoxin so administered rapidly escaped into the general circulation. Sicard, however (quoted by Hofmann), obtained better results in his experiments with dogs. The method was first used successfully in 1899 by v. Leyden, who thought this the best method of all, emphasizing the fact that the antitoxin thus came into intimate relation with blood- and lymph-vessels of the cord, and so was conveyed more quickly to the medullary cells. Whether or not antitoxin injected into the subdural space of the cord acts directly upon the cord itself, or upon the nerve roots, does not appear to have been determined. Certainly it has not been disproved, and if reasoning by analogy with tetanus toxin be allowed, it is altogether probable that antitoxin injected intraspinally is in large part absorbed into the nerve roots and the cord itself, especially if the pia or the nerve tissue is punctured. Mere withdrawal of cerebrospinal fluid by lumbar puncture has been suggested as a therapeutic measure, and it is possible that the rapid decrease in severity of the symptoms often seen may be produced in this way. It is not reasonable to expect the specific action of the antitoxin to be manifested for several hours.

Though, experimentally, treatment of tetanus by intraspinal injections of antitoxin has not been very encouraging, much more satisfactory results have been obtained in actual practice.

Hofmann reported from v. Hacker's clinic, at Graz, a series of 30 consecutive cases of tetanus. From theoretical considerations they were opposed to the intraspinal administration of antitoxin; and in the first 13 cases only subcutaneous injections were used; of these patients 7 died, a mortality of 53.8 per cent. In 3 of these

cases, 2 of them fatal, carbolic acid was also employed subcutaneously. In a fourteenth case, which also died, both subcutaneous and intraneural injections were given. Of the cases treated by subcutaneous injections only, 5 came under treatment within thirty hours of the onset of symptoms; and of these patients (mostly acute cases), 4 died, a mortality of 80 per cent.; 8 cases came under treatment more than thirty hours after the onset of symptoms, and of these only 3 patients died, a mortality of 37.5 per cent. When the fifteenth patient came under treatment, intraspinal injections of antitoxin were tried, because other treatment did not control the disease, which was of the acute type, and very severe. This patient recovered. Then in the succeeding 15 patients antitoxin was always given intraspinally; and *of the entire series of 16 patients treated by antitoxin subdurally, only 2 died*, a mortality of 12.5 per cent.; 4 of these were very acute cases, yet all recovered. In 2 cases of this latter series antitoxin was injected intraneurally as well as intraspinally.

Rogers, in a series of 7 acute cases, employed intraspinal as well as intraneural injections, and in administering the intraspinal injections he endeavored to inject at least some of the antitoxin directly into the spinal cord (intramedullary injection), so that it might reach the nerve centres as quickly as possible. Of his 7 patients, only 3 died. Of 5 patients under the care of Luckett, all the 4 who were treated by intraspinal injections recovered, while the fifth patient, not so treated, died.

In our own series of cases intraspinal injections of antitoxin were employed only in 7 patients, of whom 4 died, a mortality of 57 per cent.; but in 1 fatal case the injection was made only three hours before death, as a last resort (Case 2); in another, death was caused by a subsequent overdose of magnesium sulphate, injected into the subdural space (Case 19); and the 2 other deaths occurred in extremely acute cases (Cases 12, 13). In all the successful cases improvement was rapid (Cases 8, 10, 11).

4. *Intraneural Injections.* This method was first employed clinically by Küster in 1902. Jacobson and Pease suggested that the pressure, rather than the specific action of the antitoxin, blocked further absorption of the toxins; but an experiment in which Sawamura employed salt solution instead of antitoxin for intraneural injection, seems to disprove this supposition.

As it is a well ascertained fact that most, possibly all, of the toxin reaches the spinal cord only by travelling up its nerves, it is theoretically logical to inject the antitoxin into the nerves, in order that, like the toxin, it may reach the spinal cord and rout the enemy by the easiest road. That it will do this, when injected intraneurally, admits of no doubt in view of the overwhelming experimental evidence on the point. Just how the antitoxin acts, and by which intraneural route (axis cylinders or endo- and peri-

neurium) it reaches the cord, has not been determined. Now, though most of the toxin ascends the nerves leading from the wounded part, other lesser amounts of the toxin are simultaneously invading the cord through all the motor nerves of the body; and it is manifestly impracticable to expose and inject antitoxin into all of these nerves. Moreover, when the site of inoculation is doubtful, or unknown, uncertainty must exist as to which nerves should have injections of antitoxin. The only methods we possess for reaching all the nerves at once are (1) intravenous injections, and (2) intraspinal injections. In no case, therefore, should the surgeon depend upon intraneural injections alone, and in no case should he omit either intraspinal injections or injections into the motor nerves leading from the site of inoculation. Especially if the point of inoculation is in a muscular part, or in the upper extremity, will the main bulk of the toxin reach the cord by the motor nerves of the inoculated part; and in such cases particularly are intraneural injections requisite.

Sawamura conducted experiments to determine the relative therapeutic value of antitoxin administered *intravenously* and *intraneurally*. (1) In a first series of 4 rabbits he administered antitoxin *intravenously from eighteen to nineteen hours after toxin* had been injected intramuscularly; all 4 rabbits died of tetanus. (2) In a second series of 6 rabbits he administered antitoxin either *intraneurally alone* or *intraneurally as well as intravenously, from eighteen to twenty-four hours after toxin* had been injected intramuscularly; and although the *total amount of antitoxin* was no greater or even less than that which had been employed in his first series, yet only 2 of the rabbits died, and these deaths did not occur until the twelfth and the sixteenth days, in cases where the total amount of antitoxin was small, where it had been injected late, and where it had been given only intraneurally, and not intravenously as well. (3) In a third series of 3 rabbits he administered antitoxin *intravenously* forty hours after the intramuscular injection of toxin, and seventeen hours after the appearance of the first symptoms of tetanus; he administered antitoxin in large amounts *intravenously, intramuscularly, or subcutaneously, or by all three methods, and on several subsequent days; yet all these rabbits died of tetanus in from nine to fourteen days.* (4) In a fourth series of 4 rabbits he administered *a much less amount of antitoxin intraneurally*, after the same interval since the intramuscular injection of the toxin as in the third series; *yet not 1 of these 4 rabbits died.* In another rabbit, similarly prepared, for the sake of a control experiment, he injected salt solution into the nerve instead of antitoxin; but this rabbit died of tetanus on the ninth day.

Sawamura says (p. 85): "To increase the value of intraneural injections of antitoxin, one must strive not only to neutralize the toxin in the peripheral nerves or that which is later to reach them,

but also to bring the action of the antitoxin to bear on the toxin already in the spinal cord; and, therefore, the injection should be made into the nerve as near the cord as possible; and centrally from this point as large an amount of antitoxin as is possible must be injected." He thinks that if in his earlier experiments (the second series quoted above) he had injected the antitoxin into the central instead of into the peripheral part of the nerves, he would have had still better results.

There are few clinical reports of cases treated by intraneural injections of antitoxin; most of them are isolated cases, and hence are of little value. Küster's patient, the first so treated, recovered. Rogers has employed this plan in 7 cases, with 4 recoveries and 3 deaths, a mortality of 43 per cent. (In all these cases intraspinal injections were employed also.) Sawamura, in 1909, collected 12 isolated cases of tetanus, treated by intraneural injections of antitoxin, with only 4 deaths, a mortality of 33 per cent. In our own series of cases it was employed only twice (Cases 11 and 13), only the first patient recovering.

In the patients who have recovered after this treatment, no disability appears to have been caused except in Küster's case, where some neuritis and muscular atrophy and contractures occurred; and these may have been due to the effects of the original injury and not attributable to the treatment employed. Our own patient suffered no inconvenience from the injection made into his sciatic nerve.

5. *Intracerebral Injections.* These were originated by Roux and Borrel, who found the method valuable in experimental work: of 45 guinea-pigs thus treated, 35 recovered; whereas of 17 treated by subcutaneous injections of antitoxin only 2 recovered. But when applied to mankind, the results have been absolutely bad—not only has the mortality not been reduced, but lasting cerebral lesions have been produced in some of the patients who recovered. In 88 cases collected by v. Graff, in which intracerebral injections were used, there were 71 deaths, a mortality of over 80 per cent. Sawamura quotes the following statistics for intracerebral injections: Lambert, 52 cases, 63.43 per cent. mortality; Lereboullet, 26 cases, 67.5 per cent. mortality; Steuer, 55 cases, 67.3 per cent. mortality.

6. *Intramuscular injections* have not been employed in any large series of cases. Antitoxin injected around the wound, whether as a prophylactic or as a therapeutic agent, should be given into the muscular tissues whenever possible, to afford it a readier access to the motor nerves. As a therapeutic method intramuscular injection is better than the subcutaneous, but is perhaps inferior to the intravenous, and certainly is inferior to the intraspinal and intraneural methods.

II. FREQUENCY OF INJECTION OF ANTITOXIN. The series of cases reported by Huber has already been referred to. He thinks the antitoxin employed was of no value, and when we come to study his case reports it is quite evident that in most cases this is true. But it is true because antitoxin was not given often enough to be of any service, as well as because the total quantities were absurdly small, in view of the fact that most of it was injected subcutaneously. In 17 cases one injection alone was given, and 1 patient recovered. In 16 cases two injections were given, and 4 patients recovered. In 2 cases three injections were given, and none recovered. In 3 cases four injections were given, and 2 patients recovered. Nor is it true that multiple injections were not given because the patients did not survive long enough. Even a patient who dies in twenty-four hours after coming under treatment lives long enough to receive at least eight subcutaneous injections. When it is administered intravenously larger amounts can be given at one time, and one or at the most two injections in twenty-four hours should suffice. Intraspinal injections seldom are requisite more than once daily, and often only every third day. Intraneural injections can be repeated daily if required; this was done on three consecutive days in Case 13 of our series, but unfortunately without a successful result.

III. QUANTITY OF ANTITOXIN INJECTED. No matter what the method of injection, *the most important thing is to get the maximum quantity of antitoxin indicated into the patient's body as soon as possible.* Delay even of a few hours may determine a fatal result; 25,000 units given within the first three hours almost certainly are of more use than 50,000 units given after six hours, or given in divided doses. If one determines to use antitoxin at all, he should, we believe, make it a rule to administer it as early as possible, and *to administer the total quantity indicated as nearly as may be all at one time.* There can be scarcely any doubt that in most of the reported cases, as for example, in Huber's series, the amount of antitoxin administered has been utterly inadequate.

As already pointed out, if the injections are given *subcutaneously*, immense quantities are indicated. For an adult, with the usual acute type of case, at least 100,000 units are required in the first twenty-four hours; though a less amount may be sufficient for a child or for a comparatively mild case, one cannot be sure of the fact, and it is better to give too much than not enough. Administered *intravenously*, a less amount is sufficient; how much it is difficult to say. Probably 15,000 to 25,000 units should be administered at first, and if no effect is apparent, or if the good effect wears off, a similar amount should be given after the lapse of eighteen to twenty-four hours. If given *intraspinally*, from 3000 to 10,000 units should be given, according to the severity of the case; this need not, as a rule, be repeated in less than eighteen

to twenty-four hours. Even when administered intraspinally a certain interval must elapse before the effect of the antitoxin can be apparent. *Intraneural* injections should be made in as great amounts as the nerves will absorb. We have injected 1500 units into the sciatic nerve, all at once, on several occasions, and 750 units into each of the anterior crural and obturator nerves. If the injections are slowly made practically all of this quantity can be introduced among the nerve fibers.

CARBOLIC ACID INJECTIONS IN THE TREATMENT OF TETANUS. This method was first brought to the attention of the profession in 1893 by Bacelli, who had employed it since 1888. The well-known anesthetic properties of phenol indicate that it has an affinity for nervous tissue, and it had been used successfully by Bacelli and others in cases of neuritis before he adopted it in cases of tetanus. According to Imperiali, carbolic acid is both antibacterial and antitoxic to the *Bacillus tetani*, and acts, moreover, as a nervous sedative. He has collected 190 cases treated by Bacelli's method, with 157 recoveries and 33 deaths, a mortality of only 17.3 per cent. He classified the cases thus:

		Mortality.
Severe cases,	94, with 2 deaths and 92 recoveries.....	2.1 per cent.
Severest cases,	39, with 17 deaths and 22 recoveries.....	43.5 per cent.
Fulminating cases,	15, with 14 deaths and 1 recovery	93.3 per cent.

These statistics are open to the usual objections applicable to collected cases; and it is strange that among so large a number of case reports no cases appear which may be classed as mild or chronic in type. It may be that the Italians, recognizing that everything is comparative, class as severe those cases which we consider mild, on the theory that even a mild attack of tetanus is a severe disease. Imperiali, however, quotes Meoni as having observed 6 cases of tetanus in the past four years, all treated by carbolic injections, and with only one death. Surgeons in other countries, however, have not reported as successful results. Pearce Kintzing, almost alone in this country, reports favorable results; he treated 7 patients by carbolic injections, and all recovered; in 3 of these cases the onset of the disease was acute, in 3 the onset is not described, and in 1 the onset was very gradual. In less than half of his cases could the disease be considered very severe in type.

Bacelli's plan is to administer 1 c.c. of a 1 per cent. solution every few hours, preferably into the muscles along the spine, until 80 or 100 centigrams are given in twenty-four hours.¹² In none of the cases mentioned by Imperiali did the total amount admin-

¹² Most preparations of antitoxin in this country have added, as preservative, 0.5 per cent. of trikresol (Hitchens). Some of the foreign sera are said to contain 0.5 per cent. of phenol. Any therapeutic effect this may have must be beneficial in cases of tetanus.

istered in twenty-four hours exceed 50 centigrams. Kintzing made a 10 per cent. solution by dissolving the deliquesced crystals of phenol in sterile water; the full adult dose was 10 drops of this 10 per cent. solution (equivalent to 1 grain of pure phenol), which was diluted in 30 or 40 minims of sterile water, just before being injected. Most physicians have preferred to use a weaker solution (0.5 per cent.), and to make the injection every one or two hours, carefully watching for constitutional symptoms of carbolic acid poisoning. The tolerance of tetanus patients for carbolic acid is amazing.

Phenol injections were employed in only one patient in our series (Case 20), in conjunction with small amounts of antitoxin subcutaneously. It was a mild, chronic type of case, of puerperal origin, and though the patient survived the disappearance of all tetanic symptoms for a period of nine days, she eventually died from puerperal sepsis.

Camus has made a series of experiments to determine the comparative value of carbolic acid, magnesium sulphate, and antitoxin in the treatment of tetanus. Dogs were used, and the animals in each series received exactly the same amount of the same toxin, at the same time. These investigations show that magnesium sulphate (intraspinally) and carbolic acid (subcutaneously) have no influence on the evolution of tetanus, no matter in what amounts or at what stage of the disease they were administered. Magnesium sulphate has no other action than as a spinal depressant; and while carbolic acid possibly may have some antibacterial action, it has no effect on the fixed toxin nor on the toxin in course of fixation. Antitoxin, alone, injected simultaneously into the cerebrospinal fluid by lumbar puncture, intravenously, and subcutaneously, *gave very much better results.*

CHOLESTERIN INJECTIONS IN THE TREATMENT OF TETANUS. Experiments having shown that it is the cholesterin of the central nervous system for which tetanus toxin has special affinity, it occurred to Almagia and Mendes that hypodermic injections of this substance might neutralize the toxin. In 2 patients they used successfully injections of from 15 to 30 centigrams of cholesterin in 10 c.c. of distilled water; Pribram, however, reports the use of cholesterin in 3 patients, all of whom died. Among other substances which have been found experimentally to be capable of neutralizing tetanus toxin is urea (Sewaki).

C. The third indication in the treatment of tetanus is to *depress the functions of the spinal cord.* So far we have considered only methods to check the supply of toxin and to neutralize the toxin already formed. Now we come to an equally important factor, because even if the supply of toxin can be stopped promptly, and even if the toxin not yet firmly bound to the nerve tissues can be completely neutralized, there is in almost every case a

large amount of toxin which has become impregably entrenched in the central nervous system, particularly in the spinal cord, and *none of the methods of treatment hitherto discussed has any influence over it*. Until its action is exhausted it continues to stimulate the motor, and to a less degree, the sensory tracts of the spinal cord, and kills the patient by exhaustion. The only way to remedy this state of affairs, so far as we know, is to depress the functions of the spinal cord. We have at our disposal a number of drugs whose main therapeutic action is to render the spinal cord less susceptible to stimulus. Administration of one or more of these remedies forms an integral part of any rational plan for the treatment of tetanus. The drugs most often employed are chloral, chloretone, and similar products; the bromides; physostigma, hyoscine, morphine, and magnesium sulphate.

The usual doses of these drugs, recommended for ordinary occasions, do not apply to the treatment of tetanus. The object is to give enough of the drug to produce therapeutic action, and until this has been obtained the dose may be steadily increased. But there is one caution always to be kept in mind: this is, that the gastro-intestinal tract of a patient with tetanus may not absorb as readily as might be expected, and there is danger that drugs will accumulate in the bowels and be suddenly absorbed in overwhelming doses when a turn for the better occurs. This may be theoretical reasoning, but we are sure we have seen more deaths from tetanus with the patient completely relaxed than in convulsions. In our series of 23 cases (13 deaths) the condition at death is noted in all but 4 (Cases 1, 7, 17, 21); only 3 (Cases 4, 16, 18) died in spasm or convulsion, and 6 (Cases 2, 5, 12, 13, 19, 22) died in complete relaxation; and in some of these cases the condition was due to overaction of the spinal depressants employed.

We believe most reliance can be placed on the use of *chloral* and the *bromides*. Hutchings employed *chloretone* in 6 cases with only 1 death, and he warmly advocates this drug. It is administered by mouth or rectum in doses of from 30 to 60 grains, dissolved in whisky or in hot olive oil. In our series it was employed three times: Case 12 died after being comatose for twenty-four hours; Case 13 died after being comatose for three hours; Case 20 died from puerperal sepsis. In both Cases 12 and 13 the administration of chloretone was stopped as soon as the patients began to show signs of coma, but without avail.

Morphine as the only depressant was used in only one case in this series (Case 21), the patient dying. We believe it is less effective as a spinal depressant than chloral and the bromides, and that it never should be employed to the exclusion of these drugs. In combination with other spinal depressants it was systematically employed only in Cases 1, 5, 22, and 23, three patients dying.

Hyoscine was used in Case 15, the patient recovering.

Chloral and bromides were employed in practically all cases except Case 21, in which morphine alone was used.

Magnesium Sulphate. In 1906, Blake adopted intraspinal (subdural) injections of magnesium sulphate in cases of tetanus. The treatment is based on the anesthetic effect of intraspinal injections of this drug, as determined by Meltzer in 1905. A 25 per cent. watery solution of the chemically pure drug is employed, and 1 c.c. of the solution is used for every twenty-five pounds of body weight. In heavy adults, however, this dosage might prove excessive, as it might also in some women and young children. Fox, in 1910, collected 24 cases which had been treated by intraspinal injections of magnesium sulphate. Among these patients there were 11 deaths, a mortality of 45.8 per cent. Such isolated case reports have little value, as they give no true idea of the value of a remedy. Only when some large consecutive series of cases has been treated with magnesium sulphate can we determine its proper place in the treatment of tetanus. According to Fox's table, J. N. Henry is the physician who has had most experience with this method of treatment. He reported 4 cases, with 3 deaths, 1 of which may have been caused by magnesium-sulphate poisoning. In our own series of cases intraspinal injections of magnesium sulphate were employed in 3 instances (Cases 17, 19, 22), and all the patients died, 1 (Case 19) undoubtedly of an overdose. Other cases have been reported in which death was attributed to the remedy rather than the disease (Henry, Hessert), or in which a fatal termination was averted solely by resort to active stimulation and artificial respiration (Soutter).

Magnesium sulphate has also been used subcutaneously. Miller quotes 3 mild cases with recovery, and Paterson reports 1 successful case.

The experiments of Camus, concerning the therapeutic value of magnesium sulphate, have already been mentioned.

D. *The patient*, as well as the disease, must be treated; and we come finally to say a few words about feeding, nursing, etc. When first seen it is well to administer a purge; when the disease is once fully established, it may be very difficult to secure an evacuation of the bowels. Retention of urine must be watched for and relieved by the catheter. Isolation is desirable rather for the sake of protecting the patient from noise than for the purpose of preventing contamination of other patients, which is very rare.¹³ Slamming doors, loud and especially sudden talking, and in fact noises of all kinds should be prevented. The patient's ears may be stopped with cotton, and the floor heavily carpeted. A bed that squeaks

¹³ Reynier says that in 1902 his assistant carried spores on his ungloved hands from one hospital, where he had amputated for tetanus, to another hospital where he infected 3 patients who died of tetanus after operations by this assistant. Now that gloves are habitually worn, such an occurrence could hardly take place.

during the convulsions is a great annoyance. Window frames should be kept from rattling. Nursing must be constant and painstaking. Food must be administered at all hazards, by a nasal tube if necessary. Saline solution by the bowel, as in cases of peritonitis, tends to overcome the dehydration of the tissues produced by excessive muscular activity. Drugs may be administered in the rectal infusion, hypodermically, or by mouth.

SUMMARY. From the foregoing discussion it is evident that the rational treatment of tetanus comprises the four indications enumerated at p. 812. The *care of the wound*, both as a prophylactic and as a curative measure, is most important. The *neutralization of the toxin*, by the rational use of antitoxin, is indispensable; and we think we have demonstrated the inadequacy of the dosage usually employed for subcutaneous administration, and the necessity of intraneural, intraspinal, and probably also of intravenous injections. The excellent results reported in some quarters from the use of *carbolic-acid injections* should be remembered; it is a remedy much more readily obtainable than antitoxin. The third indication, *to depress the functions of the spinal cord*, must not be met to the exclusion of the foregoing. Those who are enthusiastic in the use of intraspinal injections of magnesium sulphate seem to forget that unless they also employ antitoxin in a rational manner they are doing nothing to aid the body tissues to withstand the onslaught of the disease. Finally, the *care of the patient*, nursing and feeding, is the most practical part of the treatment, and one without which all the other parts may fail of their effect.

When we encounter another case of tetanus, we hope to be able to apply rational treatment in the following manner:

The patient will be placed in quiet, with competent nursing facilities. As soon as possible after coming under observation, whether this be in the small hours of the night or at bright noon tide, the motor nerves leading from the wounded part will be exposed, as near to the cord as practicable, and as much antitoxin as each will contain will be injected toward the spinal cord.¹⁴ An intraspinal injection of at least 3000 units will then be made according to the usual technique for spinal anesthesia. If it is possible to prick the cord with the needle, so much the better. Next the wound of entrance of the infection will be widely opened, all foreign bodies, sloughs, etc., will be removed by forceps, scissors, or scalpel; the wound will be irrigated with hot peroxide of hydrogen, swabbed

¹⁴ For wounds of the *sole of the foot*, it is sufficient to inject the sciatic nerve; for those of other parts of the *lower extremity*, not alone the sciatic but the anterior crural and obturator nerves as well should be injected. For wounds of any part of the *upper extremity*, the brachial plexus should be exposed above the clavicle, and an injection should be made into each of its cords. These operations should be done under general anesthesia, for which we prefer chloroform. A strong linen ligature is to be looped loosely around each of the nerves exposed; the ends of these ligatures are to be left long, and used to identify the nerves and draw them up into accessible positions for the purpose of subsequent injections of antitoxin should these prove necessary.

out with 3 per cent. alcoholic solution of iodine, and loosely filled with gauze soaked in the same solution, and injection of antitoxin will be made (1500 to 3000 units) deeply into the muscular tissues around the wound. Continuous proctoclysis, as used in cases of peritonitis, will be given; and by mouth or in the rectal fluid will be administered effective doses of chloral and bromides, at appropriate intervals. Feeding will be enforced, by the nasal tube passed under chloroform anesthesia, if necessary. During the course of the first day a moderate amount of antitoxin will be administered intravenously; probably 10,000 units will suffice.

The intraneural and intraspinal injections of antitoxin will be repeated daily, under chloroform anesthesia, until marked decrease in spasticity occurs. Every twelve hours, or less often, a moderate amount of antitoxin will be injected intravenously, or even subcutaneously, so as to neutralize the circulating toxins; but the main reliance will be placed on intraneural and intraspinal injections. The administration of spinal depressants will be continued so long as they are indicated; a comatose state or muscular relaxation naturally are contraindications. The wound will be dressed daily, as above described, until a healthy granulating surface is obtained.

With such treatment, commenced within twelve hours of the first appearance of symptoms of tetanus, we believe the mortality of the disease should not be over 20 per cent. Of the 11 patients under our own care, 7 have recovered and only 4 died, a mortality of 36.36 per cent. One of these deaths was caused by an overdose of magnesium sulphate; this patient did not come under observation until the fourth day of the disease, and none of the other fatal cases came under our care until more than twenty-four hours after the onset of indubitable symptoms of tetanus.¹⁵

¹⁵ Since the above was written, one of us (Ashhurst) has seen in consultation with Dr. George W. Norris, in his ward at the Pennsylvania Hospital, another case of tetanus:

Samuel W., negro, aged twenty-seven years, crushed his right index finger shortly before December 1, 1912. The skin was broken, but he bandaged the finger himself and never had any medical treatment for it. About December 8 or 9 he began to complain of stiffness and soreness in jaws, but never had any difficulty in swallowing. On December 11 he complained of a "ball of wind" in the epigastrium, which caused oppression and dyspnea (tetanus of diaphragm?). Dyspnea became more urgent on December 13, and on December 14 he went to bed. About this time he noticed that his legs were getting stiff (descending tetanus), and could be flexed only with great difficulty; no complaint of pain. Since December 15 he has had frequent spasms (ten to twelve daily) of his abdominal and thoracic muscles. These caused no pain, but made it more difficult to breathe. His legs were not weak, and would support him if he was helped up into a standing position; but they were perfectly helpless from rigidity.

Admitted to the Pennsylvania Hospital December 17, evening. Receiving ward diagnosis: *Transverse myelitis*. Transferred to medical ward and seen by Dr. Norris on the morning of December 18, when a diagnosis of *tetanus* was made.

First seen by Dr. Ashhurst at 6.45 P.M. on December 18. No antitetanic treatment had been instituted. During the day the patient had had five general convulsions, and had a sixth convulsion while under observation. When examined after this convulsion there was *no trismus*; the head was retracted and the lumbar spine arched; the lower extremities were in full extension and very rigid. The patient lay on his right side.

December 18. At 7.30 P.M., under chloroform anesthesia, lumbar puncture was done: there was a very free flow of spinal fluid, which was under great tension (5 c.c. were sent to the labora-

The following table gives the general mortality in some recent series of consecutive cases of tetanus:

(CONSECUTIVE) CASE REPORTS.

	Cases.	Recovered.	Died.	Mortality.
Bockenheimer (1908)	20	3	17	85.0 per cent.
Busch (1907)	30	9	21	70.0 per cent.
Episcopal Hospital (1905 to 1912)	23	10	13	56.5 per cent.
Fricker (1897 to 1902)	22	9	13	55.5 per cent.
Hessert (1909)	15	5	10	66.6 per cent.
Hofmann (1907)	30	20	10	33.3 per cent.
Huber (1912)	38	7	31	81.5 per cent.
Hutchings (1909)	6	4	2	33.3 per cent.
Jacobson and Pease (1906)	191	58	133	69.6 per cent.
Kintzing (1911)	7	7	0	
Magula (1911)	33	11	21	66.7 per cent.
Simon (1911)	6	4	2	33.3 per cent.
Suter (1905)	14	2	12	85.7 per cent.

tory for examination as to presence of tetanus toxin, but through some misunderstanding this examination was not made; a culture of the fluid remained sterile); 8000 units of antitoxin (15 c.c.) were injected into the subdural space of the cord; this was all the antitoxin available at that time. The patient was given chloral, grains xv, and potassium bromide, grains xxx, every three hours by mouth.

At midnight the patient was seen again, and 15,000 units of antitoxin were given intravenously in a pint and a half of saline solution. No more convulsions had occurred.

December 19. The next morning the patient was better. There had been no more convulsions, but many opisthotonic spasms. At 7.30 A.M. he was given a sponge bath, and after this he had two general convulsions. There was more trismus than at any time, and the tongue could just be protruded between the teeth. During the forenoon chloroform was again administered, and Dr. Norris attempted to give antitoxin intraspinally, but was unable to introduce the needle. Therefore 13,500 units were given intravenously in six ounces of saline solution. This made a total of 36,500 units administered in an effective manner within sixteen hours of the time the patient came under surgical observation. No intraneural injections were given, as no facilities existed for a surgical operation.

The patient was seen again at 7 P.M. There had been no convulsions all day. His muscles were quite relaxed. The chloral was reduced.

December 20. Has had no more convulsions; only a few, and not severe, spasms. Has taken food well. Chloral stopped.

December 21. Perfectly relaxed. *Cured of tetanus.* Clear in head and converses normally, but has pneumonia at right base (probably from inspiration of food) and is quite weak.

December 22. Died at night from pneumonia; temperature, 101° F.; pulse, 148; respirations, 40.

CASES OF TETANUS AT EPISCOPAL HOSPITAL 1905 TO 1912.

Number.	Date of admission.	Age and sex.	Site of wound.	Date and nature of injury.	Incubation (time from injury to symptoms).	Time from symptoms to institution of efficient treatment.	Type of case.	Summary of treatment. Original injury.	Result.	Service of	Attending.
1	Oct. 9, '05	23, M.	Left arm	Sept. 18, '05. Vaccination.	Unknown. Less than 19 days	3 days	Severe. Convulsions early.	Neglected.	Sedatives. Antitoxin, subcutaneously (60 c.c. = 18,000 units) in 1 day.	Died, Oct. 10, '05	Sinkler and Sweeney.
2	June 4, '06	Boy	Left forearm	May 26, '06. Laceration from kick of horse.	9 days	12 hours	Severe. Convulsions early.	Ordinary antiseptic dressing.	Sedatives. Antitoxin, subcutaneously, and (3 hours before death) intraspinally (1500 units). Total amount 45,450 units in 2 days.	Died, June 6, '06	Neilson Owen.
3	Aug. 6, '06	48, M.	Right hand	Aug. 6, '06. Compound fracture of wrist-joint. (Machinery crush.)	9 days	12 hours	Mild. No convulsions.	Ordinary antiseptic dressing.	Sedatives. Antitoxin, subcutaneously, 108,000 units in 2 days.	Recovered, Aug. 23, '06	Weber and Aufhammer.
4	Mar. 5, '08	44, M.	Right toe	Jan. 9, '08. Cut by axe in felling a tree.	8 weeks	3 days	Severe. Convulsions early.	None for 5 weeks. Ordinary antiseptic dressing for 3 weeks.	Toe amputated. Antitoxin subcutaneously, 12,000 units in 1 day.	Died, Mar. 6, '08	Davis and Brown.
5	May 31, '08	26, F.	Left leg	May 31, '08. Compound fracture. Thrown into river by explosion.	Over 2 weeks	5 days, June 23, '08	Slow in onset. Convulsions late.	Ordinary antiseptic dressing.	Sedatives. Antitoxin, subcutaneously, 18,000 units in 5 days.	Died, June 30, '08. In coma 3 days before death	Neilson and Price.

6	Aug. 12, '08	13, M.	Behind ear	Aug. 6, '08. Punctured wound by rusty knife.	4 days	2 days	Mild. No convulsions.	Puncturesutured; no drain.	Antitoxin subcutaneously, 3000 units in 2 days.	Recovered, Aug. 23, '08	Deaver	Deaver and Corson.
7	Aug. 28, '08	35, M.	Foot	Aug. 24, '08. Punctured wound by rusty nail.	5 days	1 hour	Severe. No convulsions.	No treatment for 3 days, then opened and drained.	Sedatives. Antitoxin, subcutaneously, 5000 units in 2 days.	Died, Aug. 30, '08	Deaver	Deaver and Corson.
8	Sept. 28, '08	34, M.	Abdomen and thigh	Sept. 24, '08. Brush burns, hematoma. Thrown from wagon and dragged.	14 days	1 hour	Slow in onset, but severe convulsions.	Ordinary antiseptic.	Sedatives. Antitoxin, subcutaneously, (129,000 units) and intraspinally (3000 units). Total antitoxin 132,000 units in 10 days.	Recovered, Oct. 31, '08	Frazier	Ashhurst and Corson.
9	Sept. 23, '08	55, M.	Cranium	Sept. 23, '08. Gunshot fracture of temporal region and rupture of eye-ball.	4 weeks	12 hours	Mild. Slow in onset. No convulsions.	Aseptic. No operation.	Sedatives. Antitoxin, subcutaneously, (31,500 units in 8 days).	Recovered. Eyeball enucleated, Nov. 17, '08	Frazier	Ashhurst and Aufhammer.
10	Nov. 12, '08	49, M.	Foot	Nov. 4, '08. Punctured wound by rusty nail.	8 days	24 hours	Medium severity. No convulsions.	Home treatment, by ham fat, etc.	Sedatives. Antitoxin, intraspinally (3000 units), and later subcutaneously (27,000 units). Total amount, 30,000 units in 6 days.	Recovered, Nov. 18, '08	Frazier	Ashhurst and Gracey.
11	Dec. 19, '08	19, M.	Foot	Nov. 30, '08. Punctured wound by splinters from mill floor.	18 days	24 hours	Severe. Convulsion before admission.	Wound dressed twice but patient never returned for further dressings.	Three splinters removed from wound. Sedatives. Antitoxin intraspinally, and intraneurally, and into muscles around wound. Total in 2 days 4500 units.	Recovered, Dec. 31, '08	Frazier	Ashhurst and Gracey.
12	Oct. 16, '09	63, M.	Fingers	Sept. 28, '09. Lacerations by machinery.	18 days	24 hours	Severe. No convulsions.	Ordinary antiseptic dressings.	Fingers amputated. Sedatives (chlorotone). Antitoxin intraspinally, 1500 units.	Died, Oct. 19, '09 After being comatose for 24 hours	Frazier	Ashhurst and Hopper.

Number.	Date of admission.	Age and sex.	Site of wound.	Date and nature of injury.	Incubation (time from injury to symptoms).	Time from symptoms to institution of efficient treatment.	Type of cases.	Summary of treatment.		Result.	Service of	Attending.
								Original injury.	Tetanus.			
13	Nov. 20, '09	11, F.	Knee	Nov. 11, '09. Abrasion from fall.	9 days	40 hours	Slow in onset. Severe. Convulsions late.	Bread-poultice at home.	Sedatives (chlorotone). Antitoxin, intraneurally, 3 times (total 9000 units), intraspinally (1500 units), subcutaneously (3500 units). Total antitoxin 13,500 units in 3 days.	Died, Nov. 22, '09. After being comatose for 3 hours	Frazier	Ashhurst and Hopper.
14	Feb. 4, '10	45, F.	Toes	Jan. 23, '10. Laceration. Fall down stairs in bare feet.	12 days	Few hours	Mild. Slow onset. No convulsions.	Neglected for 10 days. Then iodine.	Sedatives. Antitoxin, subcutaneously, 6000 units in 3 days.	Recovered, Feb. 19, '10	Morris	Ashhurst and Siner.
15	Feb. 21, '10	23, F.	Scalp	Jan. 26, '10. Lacerated wound. Hit by brick.	19 days	1 week	Slow in onset. Severe. No convulsions.	Sutured, no drain.	Abscess opened. Sedatives. Antitoxin, intraspinally, 3000 units; subcutaneously, 21,500 units. Total antitoxin 24,500 units in 5 days.	Recovered, Mar. 8, '10	Neilson	Ashhurst and Siner.
16	July 17, '10	S. M.	Thumb	July 5, '10. Cut by hatchet.	10 days	2 days	Slow in onset. Severe. Convulsions.	Sutured, no drain.	Sedatives. Antitoxin, subcutaneously, 103,000 units in 3 in spastic state days.	Died, July 20, '10	Deaver	Griffith
17	Oct. 14, '10	7, M.	Arm	Sept. 24, '10. Vaccination.	Unknown. Less than 3 weeks	12 hours	Mild. Slow in onset. No convulsions.	Neglected.	Sedatives, and magn. sulph. intraspinally. Antitoxin subcutaneously, 60,000 units in 2 days.	Died, Oct. 16, '10	Frazier	Frazier and Henneberger.

18	Oct. 3, '10	6, F.	Arm	Sept. 7, '10. Vaccination.	Unknown Less than 24 days	3 days	Slow onset. Very severe. 2 convulsions every hour.	Treated at home by mother.	Sedatives. Antitoxin, intrinspally, 10,000 units; subcutan- eously, 45,000 units. Total antitoxin, 55, 000 units in 2 days.	Died, Oct. 5, '10 in convulsion	Frazier	Ashhurst and Griffith.
19	Feb. 4, '11	6, M.	Hand	Dec. 23, '10. Laceration. Fall on icy street.	9 days	4 days	Severe. Convulsions.	Sutured.	Sedatives and magn. sulph. intrinspally. Antitoxin, intra- spinally, 9500 units; subcutaneousy, 10,000 units. Total antitoxin, 19,500 units in 2 days.	Died, Jan. 7, '11 in perfect relaxation	Frazier	Ashhurst and Johnston.
20	Feb. 4, '11	27, F.	Uterus	Jan. 9, '11. Instrumental delivery.	Less than 22 days	4 days	Mild onset. Chronic. No convulsions.	Uterus packed for secondary hemorrhage Jan. 19, '11.	Sedatives, chlorotone, Phenol, 3 per cent. but died 9 days sol. for 1 day. Anti- toxin, subcutan- eously 26,500 units in 10 days.	Recovered, but died 9 days later (Feb. 22, '11) of puer- peral sepsis	Mutsehler	Mutsehler and Johnston.
21	Apr. 17, '11	18, M.	Fingers	Apr. 10, '11. Crush by machine.	7 days	Few hours	Severe. No convulsions.	Fingers ampu- tated.	Abscesses drained. Sedative, morphine only. Antitoxin sub- cutaneousy, 30,000 units in 4 days.	Died, Apr. 19, '11	Neilson	Alexander and Campbell.
22	Oct. 3, '11	18, M.	Scrotum	Sept. 23, '11. Punctured wound 3 inches deep from fall on rusty iron.	10 days	Few hours	Very severe. Convulsions.	No treatment.	Sedatives and magn. sulph. intrinspally. Antitoxin subcuta- neously, 59,000 units in 4 days.	Died, Oct. 7, '11	Frazier	MacFarland
23	Mar. 15, '12	28, M.	Foot	Mar. 5, '12. Punctured wound by brass bolt.	8 days	2 days	Slow onset. Severe. No convulsions.	Bandaged. No antiseptic treat- ment.	Sedatives. Antitoxin, subcutaneousy, 224,000 units in 3 days.	Recovered, Apr. 3, '12	Neilson	John.

ANALYSIS OF EPISCOPAL HOSPITAL CASES.

Twenty-three cases. Mortality, 56.5 per cent.

10 recovered (3, 6, 8, 9, 10, 11, 14, 15, 20, 23).

13 died (1, 2, 4, 5, 7, 12, 13, 16, 17, 18, 19, 21, 22).

Incubation under ten days, 11 cases. Mortality, 63.6 per cent.

4 recovered (3, 6, 10, 23).

7 died (2, 7, 13, 16, 19, 21, 22).

Incubation over ten days, 12 cases. Mortality, 50 per cent.

6 recovered (8, 9, 11, 14, 15, 20).

6 died (1, 4, 5, 12, 17, 18).

Efficient treatment within twelve hours of symptoms, 5 cases. Mortality, 20 per cent.

4 recovered (9, 10, mild cases; 11, 23, severe cases).

1 died (17, severe case).

No efficient treatment within twelve hours of symptoms, 18 cases. Mortality, 66.6 per cent.

6 recovered (3, 6, 8, 14, 15, 20, all mild cases).

12 died (1, 2, 4, 7, 12, 13, 16, 18, 19, 21, 22, severe cases; 5, mild case).

Less severe type of disease, 9 cases. Mortality, 11 per cent.

8 recovered (3, 6, 8, 9, 10, 14, 15, 20).

1 died (5).

Very severe type of disease, 14 cases. Mortality, 85.7 per cent.

2 recovered (11, 23).

12 died (1, 2, 4, 7, 12, 13, 16, 17, 18, 19, 21, 22).

Wounds of upper extremity, 9 cases. Mortality, 89 per cent.

Wounds of lower extremity, 8 cases. Mortality, 50 per cent.

Wounds of trunk, 3 cases. Mortality, 33.3 per cent.

Wounds of head, 3 cases. Mortality, 0.0 per cent.

Antitoxin used in all 23 cases.

Efficiently as to method and quantity in 12 cases. Mortality, 46.1 per cent.

7 recovered (3, 8, 9, 10, 11, 15, 23).

5 died (13, 16, 17, 18, 19).

Inefficiently in 11 cases. Mortality, 72.7 per cent.

3 recovered (6, 14, 20).

8 died (1, 2, 4, 5, 7, 12, 21, 22).

CASE HISTORIES.

CASE 1.—Edward C., aged twenty-three years. Admitted, October 9, 1905. Discharged, October 10, 1905. Died. Service of Dr. Sinkler. Attending, Drs. Sinkler and Sweeney.

Left arm was vaccinated September 18; it began to get sore in four days, and patient had slight nausea. Then felt well until October 7 (nineteen days after vaccination), when he had head-

ache, pain in back of neck, nausea, and vomiting, with beginning trismus. Family physician dressed arm and advised removal to hospital, but patient stayed home two days longer.

On Admission (third day after first symptoms) there was trismus and retraction of head, abdomen scaphoid and rigid. On arm a slough the size of a silver dollar, baring muscle, which is black and sloughing and surrounded by area of necrotic fat; no pus.

October 9. On admission, given morph. sulph., gr. $\frac{1}{4}$, at 9 A.M., 4 P.M., and 9 P.M.; tetanus antitoxin, 20 c.c. in morning, repeated in afternoon, hypodermically. At 6 P.M. there was suggestion of a convulsion.

October 10. Convulsion at 6 A.M. for four minutes. Legs rigid, slight opisthotonos; spasms at approach of anyone. Given potass. bromide, gr. xl, and chloral hydrate, gr. xxx, by enema; also morph. sulph. at 3 A.M. and 4 A.M., hypodermically. Also 20 c.c. of antitoxin. *Died*, 8 A.M.

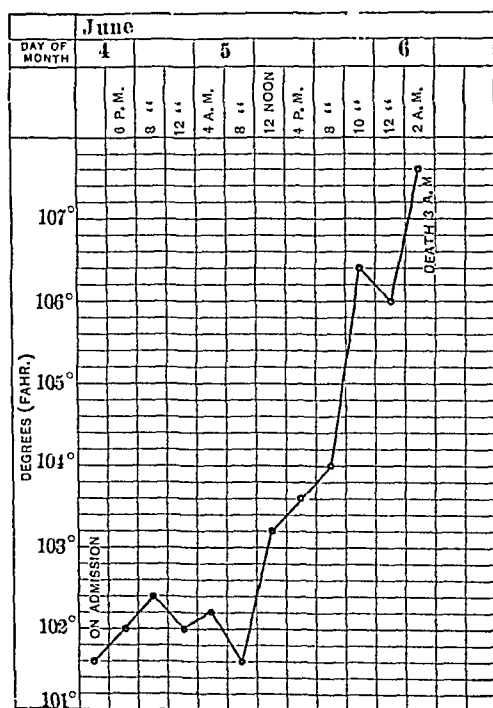


FIG. 1.—Typical temperature chart of fatal case. (Case 2.)

CASE 2.—George V., schoolboy (age unknown), under twelve years. Admitted, June 4, 1906. Discharged, June 6, 1906. Died. Service of Dr. Neilson. Attending, Dr. Owen.

On May 26, was kicked by a horse, sustaining green-stick fracture of left forearm, with lacerations of skin; not a compound fracture. Treated in surgical dispensary for the next week. On June 2 felt ill, went to bed, but was up and about the next day.

On June 4 complained of *bad pain in affected arm*, trismus and headache; had one or two slight convulsions, and was sent to the hospital

On Admission (same day as first symptoms). Jaws could be opened one-half inch; neck was stiff, abdomen rigid, legs stiff, but not rigid. Knee-jerks present on both sides, also ankle clonus. Is able to talk, has no pain until disturbed, then becomes temporarily rigid.

June 4. On admission, given bromide, gr. xv, and chloral hydrate, gr. v, every four hours by rectum. Given 30 c.c. of tetanus antitoxin every three or four hours, hypodermically.

June 5. Dose of tetanus antitoxin increased to 60 c.c. every four hours hypodermically. Given in all 330 c.c. of antitoxin hypodermically.

June 6. Given 10 c.c. of antitoxin (1500 units) intraspinally, at 12.30 A.M. *Died* at 3.15 A.M., "evidently from sudden paralysis of respiratory centres."

CASE 3.—Steven C., aged forty-eight years. Admitted, August 6, 1906. Discharged, September 2, 1906. Recovered. Service of Dr. Deaver. Attending, Drs. Weber and Aufhammer.

Right hand caught in machinery on morning of admission; diagnosis on admission, compound fracture of wrist-joint, badly lacerated and contused. Wound did fairly well.

August 15. (Nine days after injury.) Developed trismus and some stiffness of muscles of neck.

August 16. Given sodium bromide, gr. x, and chloral hydrate, gr. x, every six hours; also tetanus antitoxin, 30 c.c. every two hours hypodermically.

August 17. Given sodium bromide, gr. xv, and chloral, gr. lx, every six hours; also antitoxin as before.

August 19. Given sodium bromide, gr. xx, and chloral, gr. x, every six hours.

August 20. Sodium bromide, gr. xv, and chloral, gr. x, every six hours. Same treatment continued until

August 23. When patient developed delirium tremens, pneumonia, and later empyema. Transferred to surgical ward. *Cured of tetanus*, September 2, 1906. *Died* after many months as result of empyema.

CASE 4.—James McD., aged forty-four years. Admitted, March 5, 1908. Discharged, March 6, 1908. Service of Dr. Davis. Attending, Drs. Davis and Brown. *Died*.

Eight weeks ago, while chopping down a tree, patient lacerated his right great toe with an axe. Came to surgical dispensary five weeks later (three weeks ago). On March 2, began to have pain in back; pain and stiffness increased.

March 3. Neck and jaw became stiff. This morning the jaw became fixed. No convulsions. Walked to hospital.

On Admission. Jaws can be opened one-quarter of an inch; muscles stiff and spastic. Dr. Davis amputated the toe under ether. Patient had a convulsion during the operation.

Antitoxin, 3000 units, at 6 P.M., subcutaneously; antitoxin, 3000 units, at 10.30 P.M., subcutaneously.

March 6. Antitoxin, 3000 units, at 4 A.M., subcutaneously; antitoxin, 3000 units, at 9 A.M., subcutaneously. At 10 A.M. the patient *died of asphyxia in convulsions*.

CASE 5.—Katie M., aged twenty-six years. Admitted, May 31, 1908, at 12.30 A.M. Discharged, June 30, 1908, 5.35 P.M. Died. Service of Dr. Neilson. Attending, Drs. Neilson and Price.

Admitted for compound fracture of left tibia and fibula, simple fracture of right tibia and fibula. Injured by explosion in naphtha launch on the Delaware River, all sixteen passengers being thrown into the river. Patient badly shocked.

June 20. For some days has had slight spasticity of facial muscles and tendency to sardonic grin, more noticeable in the morning; some stiffness of muscles at back of neck; no convulsions. Sodium bromide, gr. xx, and chloral, gr. v, every four hours.

June 21. Jaws, back, and neck still stiff; facial muscles, better.

June 22. Trismus continues, but is no worse; swallows easily; says she bites her tongue whenever she sleeps.

June 23. Patient not so well; jaws stiffer; twitches more; difficulty in swallowing; neck stiff and painful. Antitoxin, 3000 units, twice (6000 in all, two hours apart). Sodium bromide, gr. xx, and chloral hydrate, gr. x, every four hours. Morph. sulph., gr. $\frac{1}{8}$, and atropine sulphate, gr. $\frac{1}{150}$, every six hours.

June 24. Antitoxin, 3000, t. i. d. (9000). Has a slight general convulsion each time disturbed.

June 25. Temperature, pulse, and respiration, rising. Temperature, 106.4° F.; comatose; sedatives stopped; sponged, p. r. n.

June 26. Conscious and restless; sedatives again.

June 27. Less restless. Antitoxin, 3000 units, at 5.30 P.M.

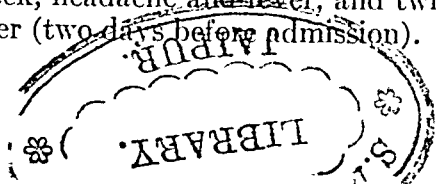
June 28. Comatose; Cheyne-Stokes respiration.

June 29. Comatose; did not move all day.

June 30. Comatose; died at 5.35 P.M.

CASE 6.—Leslie R. E., aged thirteen years. Admitted, August 12, 1908. Discharged, August 23, 1908. Recovered. Service of Dr. Deaver. Attending, Dr. Corson.

Six days before admission was struck behind the right ear with a rusty knife, which stuck in his neck; this penetrated about one and one-half inches, and was withdrawn with difficulty; small wound (punctured by thin blade); taken to another hospital where suture was put in wound and no attempt at drainage made. Began to feel stiffness at back of neck, headache and fever, and twitching of face muscles four days later (two days before admission).



On Admission. Small crust over wound behind right ear, with one silkworm gut suture; this was removed, wound opened and packed. Antitoxin, 1500 units, hypodermically.

August 13. Still slight stiffness of jaws. Antitoxin, 1500 units, hypodermically.

August 14. All muscular stiffness gone.

August 20. Out of bed.

August 23. Discharged. Diagnosis of tetanus considered positive at the time in the opinion of Dr. George Thomas (family physician) and Dr. Deaver.

November 17, 1912. Returned for examination. Has had no symptoms since. In perfect health. Small cicatrix, scarcely visible, over base of right mastoid process.

CASE 7.—Andrew H., aged thirty-five years. Admitted, August 28, 1908. Discharged, August 30, 1908. Died. Service of Dr. Deaver. Attending, Drs. Deaver and Corson.

Ran a rusty nail into his foot on August 24; came to the dispensary on August 27, because foot swelled up. Wound was opened "clear through," but is still painful, and is kept in the ward because he lives at a distance.

August 29. At 4 P.M. the patient suddenly developed stiffness of jaws and back of neck. Very much excited and irritable. Foot laid freely open where the nail had penetrated. Carbolyzed and packed. Antitoxin, 2000 units, subcutaneously. Sodium bromide, gr. xx, and chloral, gr. x, every six hours.

August 30. More opisthotonos; very restless. Antitoxin, 3000 units, hypodermically. *Died* at 10 P.M.

CASE 8.—Joseph G., aged thirty-four years. Admitted, September 28, 1908. Discharged, November 3, 1908. Recovered. Service of Dr. Frazier. Attending, Drs. Ashhurst and Corson.

Four days before admission was thrown from a wagon and was dragged, receiving a brush burn of the abdomen. Referred to ward as recent accident, because of hematoma of the left thigh.

October 6. Hematoma incised.

October 7. Jaws stiff. Antitoxin, 1500 units, subcutaneously.

October 8. Jaws still stiff; no pain except when he eats; a little twitching at night.

October 9. Stiffness in abdomen and across lower back. Jaws can be opened one-half inch. Headache all night. Antitoxin, 1500 units. Transferred to isolation ward.

October 10. At 2.30 A.M. had convulsion, tetanic in type. Threw his head back and had opisthotonos. Given chloroform and 4 c.c. of slightly turbid cerebrospinal fluid withdrawn and 3000 units of antitoxin injected. Brush burn curetted. Sodium bromide, gr. xx, and chloral, gr. xx, every six hours; 9 A.M., patient rather delirious; a little nauseated; back of neck stiff. Antitoxin, 3000

units, every four hours, subcutaneously. (Stopped October 17.)
10 A.M., jaws open one-quarter inch; some pain in head.

October 12. Headache ceased.

October 13. Abdomen much less rigid. Neck limber and back much less rigid.

October 14. Jaws open one inch.

October 17. Antitoxin reduced to 1500 units, every four hours. Sedatives decreased.

October 21. Slightly comatose.

October 24. Abdomen soft.

October 31. Sent back to ward as recovered.

CASE 9.—Thomas W., aged fifty-five years. Admitted, September 23, 1908. Discharged, December 5, 1908. Recovered. Service of Dr. Frazier. Attending, Drs. Ashhurst and Aufhammer.

A gunshot wound of the right temporal region, with a fracture of the orbit and rupture of the eyeball. Dr. G. O. Ring in consultation for the ocular condition.

October 20. Four weeks after injury. Complains of stiffness of jaws, says it started October 19; 1500 units antitoxin, hypodermically. Sodium bromide, gr. xx, every six hours. Transferred to isolation ward.

October 21. Antitoxin, 1500 units, every four hours.

October 23. Antitoxin, 1500 units, every eight hours.

October 24. Antitoxin, 1500 units, every ten hours.

October 26. Antitoxin, 1500 units, every twelve hours.

October 27. Antitoxin, 1500 units, every sixteen hours. Cured of tetanus, October 27, and transferred to convalescent ward, where Dr. Ring enucleated eyeball on November 17.

CASE 10.—John S., aged forty-nine years. Admitted, November 12, 1908. Discharged, December 8, 1908. Recovered. Service of Dr. Frazier. Attending, Drs. Ashhurst and Gracey.

Chief complaint. Stiffness of jaws and sore foot.

November 4. The patient ran a rusty nail through the shoe into his foot. Pulled the nail out and washed the foot with chloride of lime and soda ash and put ham fat on it. The foot began to swell, and he used iodine and arnica. One week after injury to the foot jaws began to stiffen so that he could not eat. Came to the dispensary and was sent to the ward November 12.

On Admission. Jaws can be opened one-half inch; right leg is rigid and painful. Has had spasms of jaws, which snap shut and cannot be opened.

November 12. At 7 P.M., under chloroform, 3000 units of tetanus antitoxin was injected into the subdural space of the cord; the foot, which meanwhile had healed, was reopened through the plantar fascia widely, and 1500 units of antitoxin injected deeply into muscles of foot; 1500 units of antitoxin injected, every four hours, hypodermically for five doses.

Summary (until morning of November 14). First day: Antitoxin intraspinally, 3000 units; into wound, 1500 units; subcutaneously, 7500 units. Total 12,000 units. Calomel, gr. ss.; mag. sulph., oz. j; whisky, fl. oz. iiij; chloral, gr. lx; potassium bromide, gr. cxx.

November 14 and 15. Second day: Antitoxin, 13,500 units, subcutaneously; chloral, gr. lx; potassium bromide, gr. clx; whisky, fl. oz. vii; calomel, gr. j; mag. sulph., oz. j.

November 15. Third day: Antitoxin, 4500 units, subcutaneously; potassium bromide, gr. lxxx; whisky, fl. oz. vss.

November 16. Fourth day: No antitoxin. No sedatives. Patient transferred to men's medical ward for bronchitis.

November 26. Patient given 3000 units of antitoxin hypodermically for pain in jaws. No further symptoms of tetanus.

November 17, 1912. Returns for examination, four years after recovery. Says for two years right foot and leg troubled him, being sometimes weak, dragging as he walked, but at other times had no trouble. In December, 1910, on stepping suddenly off a trolley car, right leg became spastic, jaws locked, and patient had to grasp a street post to prevent falling. Under great muscular effort he managed after several minutes to open his mouth. No such attack since; but occasionally had shooting pains in leg and up the spine to the head. Has been under medical treatment for the past year, and has had no trouble with his leg during that time. Until the last year has had to be laid off work for several weeks at a time once or twice annually. Physical examination is negative. Linear, supple scar on sole of right foot, two inches long. Knee-jerks normal. No paresis or spasticity.

CASE 11.—Thomas C., aged nineteen years. Admitted, December 12, 1908. Discharged, December 31, 1908. Recovered. Service of Dr. Frazier. Attending, Drs. Ashhurst and Gracey.

November 30. While running along floor of mill, soaked in machine oil, where he works, a large splinter ran through a hole in his shoe and penetrated the sole of his left foot near the head of the metatarsal of the great toe. The patient went to the dispensary, where the wound was cauterized and drained. Second visit to the dispensary two days later, but made no further visits, the patient himself removing catgut drainage that had been introduced. Was away from his work for one week.

December 17. The eighteenth day after the injury. Patient did not feel well and his jaws were sore and stiff. Took to his bed on December 18. That night he says his back muscles contracted until he rested only on the back of his head and heels. Was sent to the hospital by family physician who saw him in the morning.

On Admission. Jaws can be opened one-half inch; considerable stiffness of muscles of the back of neck and some stiffness of the back muscles; abdomen markedly rigid and a tendency to stiffness

of the legs. Wound on foot has counteropening for drainage, two inches distant. As soon as possible after admission patient was given chloroform and 3000 units of antitoxin injected intraspinaly; the wound in the foot was opened deeply through the plantar fascia, scraped out and packed with gauze soaked in iodine, 1 to 3 of water. Three splinters removed from the wound. Culture on blood serum and an anaërobic culture made (streptococci; no *Bacillus tetani*).

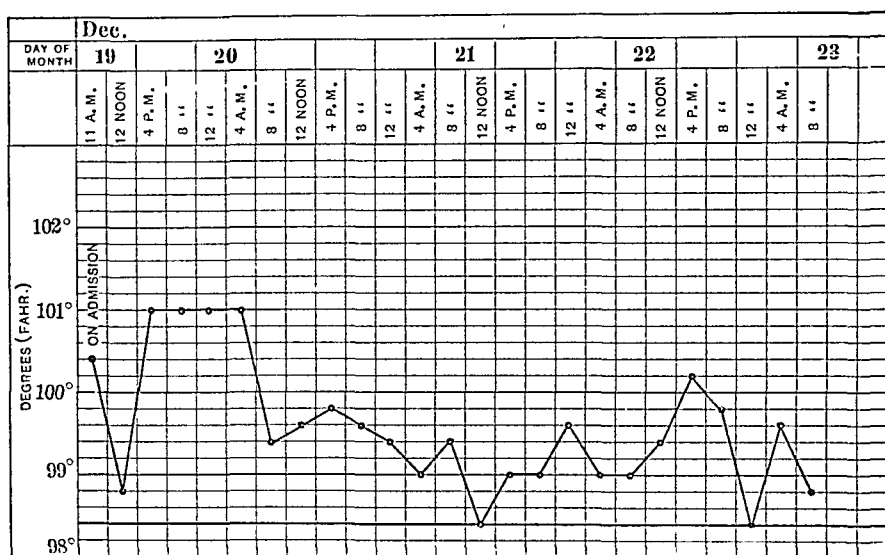


FIG. 2.—Typical temperature chart of severe case arrested promptly with ultimate recovery. (Case 11.)



FIG. 3.—Granulating wound through which antitoxin had been injected into the sciatic nerve. Wound left open for subsequent injections, which, however, were not necessary. (Case 11.)

December 20. Jaws opened one and one-eighth inches; not so stiff in the neck muscles. Chloral hydrate, gr. x, and potassium bromide, gr. xx, every three hours. Total chloral hydrate, gr. lx,

and potassium bromide, gr. cxx. At 3.30 P.M., 750 units of antitoxin was injected into the sciatic nerve, which was exposed by an incision under chloroform, and 750 units injected around the wound in the foot.

December 21. Jaws opened one and three-quarter inches. Summary: No antitoxin; chloral hydrate, gr. c; potassium bromide, gr. clx.

December 22. Summary: No antitoxin; chloral hydrate, gr. lxxx; potassium bromide, gr. clx.

December 23. Summary: No antitoxin; chloral hydrate, gr. l; potassium bromide, gr. c.

December 24. Summary: No antitoxin; chloral, gr. xxxv; potassium bromide, gr. lxx.

December 25. Summary: No antitoxin; chloral, gr. xx; potassium bromide, gr. l. Patient is now convalescent. Chloral and bromides continued in diminishing doses for three days longer.

December 31. Patient transferred to surgical ward as cured of tetanus.

CASE 12.—Francis C., aged sixty-three years. Admitted, October 16, 1909. Discharged, October 19, 1909. Died. Service of Dr. Frazier. Attending, Drs. Ashhurst and Hopper.

September 28. Fingers of the right hand badly lacerated in a picker in a woollen mill. Patient treated in the dispensary and attending daily.

October 15. Patient felt jaws becoming stiff and sent for the ambulance twelve hours later.

On Admission. October 16. General physique poor; jaws stiff; opisthotonos; abdominal muscles board-like; neck retracted; reflexes, especially the patellar, markedly increased. Chloral, gr. x, and sodium bromide, gr. xx, every two hours.

October 17. General condition poor. Under chloroform lumbar puncture was made and 1500 units of antitoxin injected. All the fingers of the right hand amputated at the metacarpal joint; even under chloroform the marked lordosis could not be made to disappear. Chloretone, gr. xxx, every two hours. Stopped the sodium bromide and chloral.

October 18. Patient semicomatose; heart bad. P.M. Heart weakening. No increase of rigidity.

October 19. Patient died at 4 A.M.

CASE 13.—Margaret D., aged eleven years. Admitted, November 20, 1909. Discharged, November 22, 1909. Died. Service of Dr. Frazier. Attending, Drs. Ashhurst and Hopper.

November 11. Patient fell and abraded right knee. Was treated at home and became infected. Jaws became stiff in the morning of November 19, but went to school and on return again called mother's attention to her stiff jaws. Went to bed and slept well. In the morning (November 20) jaws were rigidly clenched, and

when she tried to move or be moved, she became very rigid; she had pain in jaws, neck, and back. Her family physician saw her, said she had symptoms of lockjaw, left some medicine and asked to be called on the phone in the evening. When he heard her condition then he sent a note asking for the ambulance and her admission to the hospital.

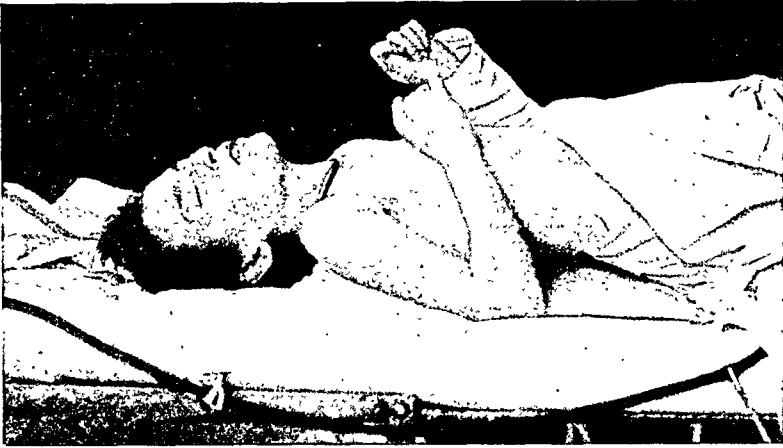


FIG. 4.—Opisthotonos. Death six hours later in convulsions. (Case 18.)

On Admission (November 20, 10.30 P.M.). Jaws were set, head retracted, legs extended and rigid; moderate lordosis; board-like scaphoid abdomen; mind clear; reflexes all increased; suppurative abrasion over tubercle of the right tibia covered with a bread poultice.

November 21, 12.30 A.M. (two hours after admission). Patient was operated upon (chloroformed.) The anterior crural and obturator and sciatic nerves were exposed and 750 units of antitoxin injected into each of anterior crural and obturator and 1500 units into sciatic; about 1500 units injected around wound in the leg, after disinfecting it and swabbing it out with 3 per cent. alcoholic solution of iodine. Continuous saline proctoclysis. Chloretone, gr. xv, every four hours by mouth. Chloral hydrate, gr. xx, and sodium bromide, gr. xxx, every two hours by rectum in saline proctoclysis. During the morning (November 21) the patient was quiet, jaws slightly less rigid and can now open one-quarter of an inch. Seems better generally.

2.30 P.M. Incisions reopened and same dose of antitoxin injected into anterior crural, obturator, and sciatic nerves; 1500 units of antitoxin given intraspinally under chloroform.

4.30 P.M. Teeth can be separated further.

7.30 P.M. Patient not so well. Temperature, pulse, and respiration all rising.

10.30 P.M. Patient restless. Jaws still less rigid. Clonic contractions of muscles of back and legs every few minutes; 1500 units of antitoxin hypodermically.

November 22, 1.30 A. M. No change.

9.30 A.M. Patient weaker. Chloretone stopped. Tincture of digitalis, minims v. Camphorated oil, minims xx, every four hours.

12.00 P.M. Antitoxin as above into nerves under chloroform; none given intraspinally.

3.00 P.M. Patient has been comatose ever since chloroform this noon. Respirations shallow and labored. Pulse better.

6.30 P.M. Patient died, in relaxation.

CASE 14.—Sarah McV., aged forty-five years. Admitted, February 4, 1910. Discharged, February 19, 1910. Recovered. Service of Dr. E. J. Morris. Attending, Drs. Ashhurst and Siner.

January 23 (twelve days before admission). When pregnant three months, fell down stairs in bare feet and sprained back and received small lacerated wound between fourth and fifth right toes; no other injuries. The interdigital cleft became very painful the next day and the foot began to swell. Patient treated the foot at home for ten days and then on February 2, came to the surgical dispensary and was dressed. Returned two days later and complained of pain on opening mouth and stiffness of jaws. Referred at once to isolation by Dr. Ashhurst, after renewed antiseptic treatment of wound with iodine (3 per cent.).

On Admission, February 4. Chief complaint: Stiffness of jaws and neck and wound of right foot.

Examination. Reflexes slightly increased; no ankle clonus or Babinski; abdomen not rigid; patient three months pregnant; 3000 units of antitoxin subcutaneously on admission. Potassium bromide, gr. xxx, and chloral hydrate, gr. xv, every four hours. Mag. sulph., oz. ss.

February 5. Patient complains of headache, backache, and muscular pains all over; abdomen somewhat tender and rigid. Reflexes slightly increased; 1500 units of antitoxin, one-half around wound in foot and one-half in abdominal wall, hypodermically. Bromides and chloral only t. i. d.

February 6. Pains in pelvis; uterine bleeding all day, passing several large clots.

Pelvic examination: Large soft cervix; fundus above pubis; os not dilated.

February 7. At 2 A.M. a very profuse metrorrhagia. Os now patulous and placenta protruding. Uterus cleaned out with placental forceps and packed. Fluid extract of viburnum prunifolium, dram j every three hours.

10.00 A.M. Patient in good condition.

February 8. Packs removed; 1500 units of antitoxin subcutaneously.

February 19. Patient has done well. Discharged today as cured of tetanus.

CASE 15—Mary S., negro, aged twenty-three years. Admitted, February 21, 1910. Discharged, March 8, 1910. Recovered. Service of Dr. Neilson. Attending, Drs. Ashhurst and Siner.

January 26, at 2 A.M., while walking on the street, the patient was struck on the head by a brick, causing a slight laceration. She was taken in the ambulance to another hospital, where the laceration was sutured and the patient discharged one hour later. Returned on the tenth day and had the sutures removed. She says that at that time there was a small tender swelling in the wound.

February 14. One week before admission, and nineteen days after the wound, the patient's jaws gradually became painful, and she began to have difficulty in opening her mouth. The condition gradually grew worse, and she can now barely separate her jaws one-quarter of an inch, with much pain.

On Admission, February 21. Temperature, 100° F. Chief complaint is stiffness of jaws. Postauricular lymph nodes on right enlarged. Cicatrix from recent wound on scalp, nearinion; below is a small, tender lump. Abdomen a little tender. Some rigidity of muscles of back and neck. Patellar reflexes greatly exaggerated on the right and increased on the left. No ankle clonus or Babinski. Mag. sulph., oz. ss., stat. Antitoxin, 3000 units subcutaneously on admission and 1500 units intraspinally. Potassium bromide, gr. xxx, and chloral hydrate, gr. vii, every three hours by mouth. Hyoscine, gr. $\frac{1}{100}$, hypodermically, 3 P.M. and 11 P.M. Abscess on scalp opened.

February 22. Antitoxin 3000 units subcutaneously at 10 A.M. Sedatives as before. Patient's condition not so good. Jaws nearly closed. Neck and back somewhat rigid. Stuporous, and mind wanders. More pain in head. Antitoxin, 3000 units, at 4 P.M., subcutaneously; 1500 units at 8 P.M., when there was some improvement. Jaws not so rigid.

February 23. 10 A.M., 2 P.M., and 8 P.M., 1500 units of antitoxin subcutaneously. Condition the same. Morphine, gr. $\frac{1}{8}$. Great pain, worse in the back. Sedatives as before.

February 24, A.M., and P.M., 1500 units of antitoxin subcutaneously. Jaws opened one-half inch in the morning, and open one inch by evening. Sedatives as before.

February 25. No more sedatives after February 24; 1500 units of antitoxin subcutaneously. Tincture of digitalis, minims x, t. i. d.

February 26, 3000 units of antitoxin subcutaneously. Pains in lower jaw.

February 27. No antitoxin after this date.

February 28. Patient can flex neck until chin is within two inches of chest.

March 1. Can make chin touch chest.

March 2. Sat up in bed for first time. Soft diet for first time.

March 3. In chair for one-half hour.

March 4. Jaws open three-eighths of an inch.

March 5. In chair for two hours.

March 6. Patient walked a little.

March 7. Jaws can be opened one-half inch. Neck still somewhat rigid, and when it is flexed until chin touches sternum she has some pain in the back.

March 8. Discharged as cured.

CASE 16.—Charles M., aged eight years. Admitted, July 17, 1910. Discharged, July 20, 1910. Died. Service of Dr. Deaver. Attending, Dr. Griffith.

July 5. Was cut on right thumb by hatchet. Wound was dressed in dispensary, using three sutures. No symptoms until Friday evening, July 15, when he complained of a little difficulty in swallowing. On July 16, felt all right. On July 17, before admission, had a spasm which lasted only a few minutes.

On Admission. Patient perfectly relaxed, with the exception of some slight stiffness of jaws, and a sardonic grin, which was marked. Given 43,000 units of antitoxin hypodermically. Chloral, gr. ij, and potassium bromide, gr. vi, by mouth, every three hours. Had three spasms on day of admission, each lasting about three minutes, after which he was relaxed.

July 18. Temperature higher. General condition not so good. Better toward night. Five spasms during the day, each about three minutes, one severe. Opisthotonos marked in last convulsions and relaxation afterward not so complete. Sweating is marked; 5000 units of antitoxin, every three hours, for eight doses—40,000 units, hypodermically. Bromide and chloral as before.

July 19. General condition good, but jaws more locked. Some difficulty in swallowing. Pain in abdomen. Cyanosis of lips marked during spasms. Four spasms today, one quite severe; 20,000 units of antitoxin.

July 20. General condition not so good. Jaws locked. Took a bad turn at 9 P.M. Temperature, 106° F. Died at 10.30 P.M.

CASE 17.—Harry F., aged seven years. Admitted, October 14, 1910. Discharged, October 16, 1910. Died. Service of Dr. Frazier. Attending, Dr. Henneberger.

Three weeks ago the patient was vaccinated, and was all right until the evening of October 13, when malaise was noted and he complained of stiffness of back and soreness in jaws. Brought to the hospital the next morning.

Examination. Jaws somewhat stiff and unable to open mouth to full extent. Abdomen scaphoid, with great rigidity of abdominal muscles. The least tapping throws them into a tetanic contraction; 5000 units of antitoxin, every four hours, subcutaneously. Mag. sulph. (intraspinal), 2 c.c. of 25 per cent. solution at 12.30 A.M., October 15.

October 16. Died at 1 A.M. Temperature, 104° F. Total amount of antitoxin in two days, 60,000 units subcutaneously.

CASE 18.—Minnie P., aged six years. Admitted, October 3, 1910. Discharged, October 5, 1910. Died. Service of Dr. Frazier. Attending, Drs. Ashhurst and Griffith.

September 7. Patient was vaccinated. She did well. Scab formed, which was knocked off at play and no other scab formed. Mother dressed the wound and a slight infection occurred, but healing proceeded normally from outside toward the centre. No untoward occurrence until October 1, when the child complained of mouth being sore, but was able to eat and play and slept well the night of October 1. Complained of mouth all of October 2, but could swallow, and went to Sunday school. On Monday, October 3, had malaise, and a weak spell in which she fell and received an ugly contusion on forehead. During the day she still complained of mouth being sore and some slight stiffness. General muscular rigidity noticed, and jaws were somewhat hard to open. Brought to the hospital on the night of October 3.

On Admission. Contusion on the forehead the size of an orange, received by a fall in a weak spell. Opisthotonos; sardonic grin marked; angles of mouth drawn down; muscular rigidity marked; complains of pain in stomach; head retracted; had one slight convulsion before admission; sent to isolation ward, October 4; 5000 units of antitoxin subcutaneously on admission.

October 4. Muscular rigidity marked; opisthotonos and sardonic grin marked. Patient able to swallow. Had about two convulsions an hour today, but very slight. Potassium bromide, gr. lx, and chloral, gr. xxx, every three hours; 25,000 units of antitoxin subcutaneously.

October 5. Seen by Dr. Ashhurst on this date first; 10,000 units of antitoxin intraspinally, and 15,000 units of antitoxin subcutaneously. Temperature rising. Convulsions increasing in severity. Patient is very restless, but able to take nourishment and medicine. A very severe convulsion at 3 P.M., followed by two slighter ones. Temperature, 106° F. At 4 P.M. several slight convulsions; breathing very labored; cold, clammy sweat. At 5.30 P.M. had three very severe convulsions, and died at 5.45 P.M. Temperature, 106.6° F.

CASE 19—Thomas B., aged six years. Admitted, January 4, 1911. Discharged, January 7, 1911. Died. Service of Dr. Frazier. Attending, Drs. Ashhurst and Johnston.

Patient has a tapeworm, and has lost weight in the last few months. On December 23, while running in the street, he fell over a Belgian block, striking the palm of the right hand against a sharp piece of ice. A U-shaped laceration at the thenar eminence resulted, which bled very profusely. Was taken to another hospital, where two sutures were inserted, which controlled the hemorrhage. No antitoxin was given.

January 1. It was first noticed that his jaw was stiff and that he spoke like a child who was tongue-tied. He was taken back to the same hospital, where, on account of the difficulty in opening the mouth and some patches on the tongue, diphtheria was suspected, but by mouth gag no membrane was found in the throat.

January 4. A positive diagnosis of tetanus was made, and he was sent to the Episcopal Hospital.

On Admission. Teeth cannot be separated more than one-half inch. Face is wrinkled and angles of the mouth are drawn down and out in a sardonic grin. Depressors of the jaw become tense on any attempt to open mouth. When the patient is quiet, nothing abnormal is apparent. Neck muscles and those of the back are a little stiff, but no opisthotonos is present. Limbs are normal. A clean granulating wound on the right thenar eminence. 12 midnight; 5000 units of antitoxin in right forearm.

January 5, 4.00 A.M. Chloral hydrate, gr. iij.

6.00 A.M. Slight convulsion.

8.00 A.M. Jaws more rigid.

9.00 A.M. 5000 units of antitoxin intraspinally.

1.30 P.M. Potassium bromide, gr. v. Weaker. Delirious. Temperature, 104° F.

4.00 P.M. Chloral hydrate, gr. iij. Patient sleeping.

8.00 P.M. 5000 units of antitoxin subcutaneously. Potassium bromide, gr. v.

12.00 P.M. Chloral, gr. iij. Temperature, 103.4° F.

January 6, 4.00 A.M. Potassium bromide, gr. v. Temperature, 100.2° F.

12.00 M. 4500 units of antitoxin intraspinally. Seen by Dr. Ashhurst on this date first.

1.00 P.M. Potassium bromide, gr. v. Temperature, 101.8° F. Chloral, gr. iijss by rectum.

4.00 P.M. Sleeping quietly.

8.00 P.M. Potassium bromide, gr. v, and chloral, gr. ijss by rectum, which was expelled.

9.00 P.M. Potassium bromide, gr. v, and chloretone, gr. v.

11.00 P.M. Sleeping.

January 7, 1.00 A.M. Chloretone, gr. v, because he awoke.

3.00 A.M. Potassium bromide, gr. v. Temperature, 100.4° F.

9.00 A.M. Potassium bromide, gr. v.

12.00 M. Temperature, 101° F.

2.00 P.M. Mag. sulph., $3\frac{3}{4}$ grams in a 25 per cent. solution intraspinally (7 c.c. of solution, clearly an overdose).

3.00 P.M. Patient died in perfect relaxation. Probably would have recovered if no magnesium sulphate had been given.

CASE 20.—Lillie S., aged twenty-seven years. Admitted, February 4, 1911. Discharged, February 22, 1911. Recovered. Service of Dr. Mutschler. Attending, Drs. Mutschler and Johnston.

Personal History. Has had one child. A prolonged and difficult labor with a laceration of the cervix. During the present gestation health has been good. Much better than previously.

Present Condition. January 9. While at breakfast, had a sudden profuse hemorrhage. The uterus was evacuated by her physician. Improved for ten days, when a second sudden very severe hemorrhage occurred. Two days later developed phlebitis in the left leg. Twenty-two days after delivery, four days before admission, patient began to have dull pains in muscles at back of neck, some difficulty in separating jaws, and slight pain on deglutition; all symptoms increased slowly in severity daily. On the day before admission had 5000 units of antitoxin subcutaneously.

On Admission. Able to open incisor teeth only enough to admit tip of the index finger. This causes some pain in the neck. Some rigidity of muscles of back of neck, and pain on motion. Uterus felt just above pubis.

Vaginal Examination. Small amount of brownish discharge, not especially foul. Cervix soft and lacerated; uterus enlarged, soft, not freely movable. Left leg uniformly increased in size; skin glistening, pits slightly on pressure. No pain in leg or on pressure over veins.

February 4, 6.00 P.M. Chloretone, gr. x, every four hours.

8.00 P.M. 5000 units of antitoxin in pectoral muscle. Left leg bandaged.

February 5, 8.00 A.M. Good bowel movement; appetite good; considerable thirst. Unable to open jaws enough to admit spoon.

4.00 P.M. Phenol, 3 per cent., minims, xv, every two hours, hypodermically.

8.00 P.M. Antitoxin, 5000 units, in right pectoral muscle. Patient very drowsy. Pain less in the neck.

February 6, A.M. Patient very drowsy.

4.00 P.M. Temperature, 104.8° F.; pulse, 136; respiration, 28.

5.00 P.M. All treatment stopped. Atropine sulphate, gr. $\frac{1}{100}$; morph. sulph., gr. $\frac{1}{8}$, hypodermically.

8.00 P.M. All appearances of intense sepsis. Completely relaxed. No pain anywhere. Infusion of digitalis, fl. dr., ij. Enteroclysis with normal salt solution, to take one pint every three hours; with each pint, two drams infusion of digitalis.

February 7, 12.00 A.M. Antitoxin, 5000 units, subcutaneously. Return of pain and stiffness. Chloretone, gr. x, every three hours.

February 10. 5000 units of antitoxin subcutaneously.

February 11. 5000 units of antitoxin.

February 13. 1500 units of antitoxin.

February 22. Patient gradually improved until morning of February 22, when all tetanic symptoms had been absent for some days. On latter date, she had a severe uterine hemorrhage. Uterus packed, but patient failed rapidly.

February 23, 12.15 A.M. Patient died.

CASE 21.—Poland P., aged eighteen years. Admitted, April 17, 1911. Discharged, April 19, 1911. Died. Service of Dr. Neilson. Attending, Drs. Alexander and Campbell.

April 10. While at work the patient had his hand caught in a machine; index, ring, and middle fingers cut. Middle and ring fingers amputated on the same day. Discharged on April 14. Returned to hospital on April 17, with tetanus. Jaws locked, pain in back, and stiffening of neck muscles. Hand is very much swollen, and has a very offensive odor. Stitches removed from fingers. Palm of hand opened up and one fluidounce of pus removed. Several stab wounds made on back of hand; 5000 units of antitoxin given subcutaneously every seventh hour. Hand dressed every day. Continuous 1 to 5000 bichloride dressing on hand.

April 17. Antitoxin, 10,000 units, subcutaneously; whisky, oz. j, and morph. sulph., gr. $\frac{1}{4}$.

April 18, A.M. Antitoxin, 5000 units, subcutaneously; whisky, oz. jss, and morph. sulph., gr. $\frac{1}{4}$; P.M. Antitoxin, 10,000 units, subcutaneously; whisky, oz. ij, and morph. sulph., gr. $\frac{1}{4}$.

April 19. Patient died at 3.55 A.M.

CASE 22.—John McD., aged eighteen years. Admitted, October 3, 1911. Discharged, October 7, 1911. Died. Service of Dr. Frazier. Attending, Dr. MacFarland.

September 20. The patient fell on a rusty hydrant stalk; the stem entered the scrotum, and he walked home untreated. Later on the same day he came to the surgical dispensary, where he was not treated, but referred to ward, but did not stay. No antitoxin given. Thirteen days later was admitted to the hospital with symptoms of tetanus. (How long these had existed is not stated; probably two days.)

On Admission. Well-developed adult male. Temperature, 99° F.; pulse and respiration, normal. Has a sardonic grin; head retracted; slight opisthotonos; occasional attacks of general rigidity; jaws can be opened one-half inch; over pubis in the midline is an area the size of a quarter dollar, which is tender, red, and inflamed; open wound on left side of scrotum, discharging yellow, purulent material. Probe reaches from here to area above pubis under the skin.

Treatment. Under local anesthesia, incision made over tender area at pubis, and through-and-through drainage to scrotal wound

with rubber tube. Antitoxin, 14,000 units in 5000 doses subcutaneously. Potassium bromide, dram ij, and urotropine, gr. x.

October 4. Patient is worse. Frequent attacks of spasms, and pulse and respiration have increased. Antitoxin given every six hours, to make 20,000 units, subcutaneously. Frequent convulsions, with opisthotonos lasting two to three minutes. Potassium bromide, drams ix; urotropine, gr. x; morph. sulph., gr. $\frac{1}{4}$.

October 5. Potassium bromide, drams ivss, and urotropin, gr. v. Antitoxin, 10,000 units, subcutaneously. Morph. sulph., gr. $\frac{3}{4}$; intraspinal injection of mag. sulph., 25 per cent. solution, 6 c.c.

October 6. Patient has developed pneumonia, and is in a critical condition. No convulsion since early morning. Antitoxin, 15,000 units, subcutaneously. Potassium bromide, drams ijss; urotropin, gr. xv; atropine, gr. $\frac{1}{75}$; mag. sulph., intraspinally, 3 c.c. of a 25 per cent. solution; whisky, oz. iiiss; tincture of digitalis, minims xl, hypodermically, in 10-minim doses.

October 7. Patient in very critical condition. Died at 6 P.M.

CASE 23.—Gregol S., aged twenty-eight years. Admitted, March 15, 1912. Discharged, April 20, 1912. Cured. Service of Dr. Neilson. Attending, Dr. John.

Chief complaint is rigidity of jaw and neck muscles; wound of right foot.

March 5. The patient ran a piece of a brass bolt into the outer side of his foot, and went to a "lodge doctor," who bandaged it without any further treatment. Eight days later, on Wednesday, March 13, began to have pain and rigidity of muscles of jaw and neck. Was admitted on Friday night, March 15, with well-marked trismus and considerable rigidity and retraction of neck with moderate arching of the back.

On Admission. Symptoms as above. Face is drawn, mouth particularly being drawn at the corners into the typical tetanic risus sardonicus. The head is rigid and well drawn back. Complains of some pain in the neck and thorax. Is able to separate the teeth about one inch.

Thorax: Lungs negative. Heart area normal and sounds good. No murmurs. Back arched from occiput to buttocks, but the legs are freely movable. Centre of arch about three inches above the bed.

Abdomen: Board-like rigidity of all the abdominal muscles, increased on examination. A small inguinal hernia on right side.

Extremities: All are normal, with the exception of the right leg, which shows a penetrating wound on the outer side of the right foot about the middle of the arch. This runs up and back under the skin below the external malleolus for about three inches.

March 15. Wound in foot opened its whole length; slough cut away; washed with peroxide and warm boric, and packed with iodoform gauze; 6000 units tetanus antitoxin injected subcuta-

neously. Chloral hydrate, gr. xx, and potassium bromide, gr. x, every four hours, with morph. sulph., gr. $\frac{1}{8}$, hypodermically, every four hours.

March 16. 93,000 units of antitoxin injected subcutaneously. Patient is not so well. Can barely separate teeth, and has convulsive spasms every few seconds. No real convulsion, however.

March 17. 65,000 units of antitoxin injected subcutaneously. Patient can open mouth a little wider, but the convulsive spasms keep up, and there is more rigidity and arching of the back.

March 18. 60,000 units of antitoxin injected subcutaneously. Patient in about the same condition. No worse.

March 19. No antitoxin. Patient has had first real sleep this morning. Slept again for several hours in the afternoon. Convulsive spasms are not quite so frequent, nor so severe. Arching and rigidity not diminished, possibly slightly increased.

March 24. Patient is much improved, and rests quietly. Bromide and chloral reduced by half.

March 26. Patient rests quietly, but rigidity continues undiminished, and considerable urticaria over body. Given soft-boiled egg and a small piece of dry toast for dinner.

March 27. Rigidity considerably decreased, patient in good condition.

March 30. Patient's general condition is good. Rigidity is well marked but decreasing slowly; most marked in abdominal muscles. Blood pressure of left arm: systolic, 182; diastolic, 124.

March 31. Hot bath for fifteen minutes seemed to decrease rigidity to a considerable extent. Returned later in the day, but the patient was much more comfortable.

April 3. Transferred to convalescent ward.

April 7. Patient is doing well, and is up and in chair daily.

April 16. Patient put on full diet. Is up and walking about the ward. Is still a little weak, and is slightly sore in the chest, but on the whole is in good condition.

April 20. Patient is up and about. Still has slight soreness over lower thorax. Discharged in good condition.

November 17. Returned for examination. No symptoms since recovery, and in excellent health now.

REFERENCES.

- Almagia and Mendes. *Internat. Clinics*, Philadelphia, 1908, iii, 12.
 Bacelli. *London Med. Mag.*, 1893-'94, ii, 811.
 Beates and Thomas. *Monthly Cyclop. and Med. Bull.*, 1911, iv, 326.
 Blake. *Surg., Gyn., and Obst.*, 1906, i, 541.
 Bockenheimer. *Arch. f. klin. Chir.*, 1908, lxxxvi, 277.
 Busch. *Arch. f. klin. Chir.*, 1907, lxxxi, 27.
 Camus. *C. R. Soc. de Biol.*, Paris, 1912, lxxii, 109.
 Dehne and Hamburger. *Wien. klin. Woch.*, 1904, xvii, 807.
 Donitz. *Deutsch. med. Woch.*, 1897, xxiii, 428.

- Fedden. *Clin. Jour.*, 1911, xxxvii, 356, Case 2.
 Fink. *Jour. of Trop. Med.*, 1911, xiv, 161.
 Fox. *New York Med. Rec.*, 1910, ii, 720.
 Frazier. *Keen's Surgery*, Philadelphia, 1906, i, 478.
 Fricker. *Deutsch. Zeit. f. Chir.*, 1907, lxxxviii, 429.
 v. Graff. *Mitth. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxv, 145.
 Gumprecht. *Deutsch. med. Woch.*, 1894, xx, 546.
 Gumprecht. *Arch. f. d. ges. Physiol.*, 1894, lix, 105.
 Hessert. *Surg., Gyn., and Obst.*, 1909, ix, 145.
 Hitchens. *American Vet. Rev.*, August, 1910.
 Hofmann. *Beitr. z. klin. Chir.*, 1907, lv, 697.
 Huber. *Beitr. z. klin. Chir.*, 1912, lxxvii, 139.
 Hutchings. *Surg., Gyn., and Obst.*, 1909, ii, 11.
 Imperiali. *Giorn. di med. Milit.*, 1910, fasc. x to xi; in *Policlinico*, 1911, xviii, 363.
 Jacob. *Blumenthal and Jacob: Berl. klin. Woch.*, 1898, xxxv, 1079.
 Jacobson and Pease. *Trans. Amer. Surg. Assoc.*, 1906, xxiv, 254.
 Kintzing. *New York Med. Jour.*, 1911, xi, 1268.
 Krauss and Amiradzibi. *Zeit. f. Immunitätsforsch.*, 1910, vii, 1.
 Küster. *Centr. f. Chir.*, 1905, xxxiii, Beil., S. 15.
 Lop. *Bull. Soc. Chir.*, Paris, 1906, xxxii, 184.
 v. Leyden. *Berl. klin. Woch.*, 1899, xxxvi, 632; *Deut. med. Woch.*, 1901, xxvii, 477.
 Luckett. *Med. and Surg. Repts., Bellevue and Allied Hosps.*, New York, 1904, i, 319.
 Magula. *Beitr. z. klin. Chir.*, 1911, lxxvi, 588.
 Maunoury. *Assoc. Franc. de Chir.*, 1902, xv, 608.
 Marie and Morax. *Ann. de l'Inst. Pasteur*, 1902, xvi, 818; 1903, xvii, 335.
 Matas. *Trans. Amer. Surg. Assoc.*, 1909, xxvii, 40.
 McCampbell. *Jour. Amer. Med. Assoc.*, 1907, i, 919.
 McFarland. *Jour. Amer. Med. Assoc.*, 1903, ii, 34.
 Meyer and Ransom. *Arch. f. exp. Pathol. u. Pharm.*, 1903, xlix, 369.
 Miller. *AMER. JOUR. MED. SCI.*, 1908, ii, 781.
 Neary. *New York State Jour. of Med.*, 1910, x, 476.
 Nissen. *Deutsch. med. Woch.*, 1891, xvii, 775.
 Nocard. *Bull. Acad. de Méd.*, Paris, 1895, xxxiv, 407.
 Palmer. *Jour. Royal Army Med. Corps*, 1912, xviii, 400.
 Paterson. *Lancet*, 1910, i, 922.
 Porter and Richardson. *Boston Med. and Surg. Jour.*, 1909, clxi, 927.
 Pribram. *Prag. med. Woch.*, 1908, xxxiii, 719.
 Remertz. *Inaug. Dissert.*, Berlin, 1911. Ueber prophyl. Injektion von Tetanus Antitoxin.
 Reynier. *Bull. Acad. de Méd.*, Paris, 1908, lix, 623, 629, 780.
 Riche. *Bull. et Mém. Soc. Chir.*, Paris, 1912, xxxviii, 476.
 Rogers. *Jour. Amer. Med. Assoc.*, 1905, ii, 12.
 Roux and Borrell. *Ann. de l'Inst. Pasteur*, 1898, xii, 225.
 Sawamura. *Arbeiten a. d. Inst. z. Erforschung d. Infektionskrankh. in Bern (Kolle)*, Heft iv, 1, Jena, 1909.
 Schnitzler. *Centr. f. Bakteriöl.*, 1893, xiii, 679.
 Sewaki. *Sei-i-Kwai Med. Jour.*, Tokyo, 1910, xxx, 33.
 Simon. v. Graff: *Mitth. a. d. Grenzgeb. d. Med. u. Chir.*, 1912, xxv, 145.
 Solieri. *Centr. f. Bakteriöl.*, 1910, lv, 141.
 Suter. *Arch. f. klin. Chir.*, 1905, lxxv, 113.
 Stintzing. *Münch. med. Woch.*, 1898, xlv, 1265.
 Stintzing. *Mitth. a. d. Grenzgeb. d. Med. u. Chir.*, 1898, iii, 461.
 Tarozzi. Cited. by Solieri, q. v.
 Vaillard. *Bull. Acad. de Méd.*, Paris, 1908, lix, 569, 587.
 Vincent. *Ann. de l'Inst. Pasteur*, 1904, xviii, 748; *Soc. de Biol. de Paris*, in *Gaz. des Hép.* 1908, lxxxi, 620, 668, 921.
 Zupnik. *Deutsch. med. Woch.*, 1900, xxvi, 837.

ISOLATED SCLEROTIC INVOLVEMENT OF THE MITRAL VALVE.

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THE frequency of occurrence of mitral-valve deformity and disease independent of and in the absence of other cardiac-valve implication, is one that has received attention only, as a rule, from the standpoint of vegetative endocarditis. It has been described customarily as rheumatic in origin, and at least in its acute forms has been regarded as a part of true bacterial rheumatic disease.

Sclerotic thickening and deformity, causing insufficiency or stenosis, and oftentimes both anatomic effects, have received scant attention at the hands of students of the heart, and perhaps less than has been merited by their actual frequency and interest. Both in the wards of the Philadelphia Hospital and in the autopsy opportunities of private practice I have been impressed by the sclerotic nature of occasional mitral lesions, which I had been led by the history of the case during life and its course while under my observation, to regard as subacute recrudescences of a bacterial endocarditis of a vegetative type. Usually the physical signs have indicated mitral insufficiency or mitral stenosis, or both. Less frequently the indications have been those of purely aortic disease. Irrespective of the location my attention has been attracted by the sclerotic nature of the process and the necessity of inquiring whether I had erred in my understanding of its etiology. I confess that with each new instance, in spite of the association of tonsillitis, joint symptoms, or even pericardial inflammation, I have been forced to look away from acute rheumatism as a satisfactory explanation of the lesion, and to search for a more likely immediate cause.

In this brief study I will refer only to the sclerotic changes of the mitral valve that occur in the absence of apparent lesions of the other cardiac valves. In a later communication I hope to point out the significance of similar processes limited to the aortic valve.

THE ANATOMICAL LESION. I have already referred to the fact that I have at autopsies studied examples of sclerotic insufficiency, also of the frequent combination of sclerotic stenosis with insufficiency of the mitral valve. I have never seen such a stenosis in the absence of an accompanying anatomical insufficiency, though not always of such a character as to furnish the classical auscultatory signs. I have observed a fibrosclerotic insufficiency in the absence of a deformity amounting to an anatomical stenosis, though far less regularly did the patient during life show either the physical

signs or the symptoms of valvular obstructive disease. The photographs are illustrative of the isolated sclerotic involvement of the mitral vavles.

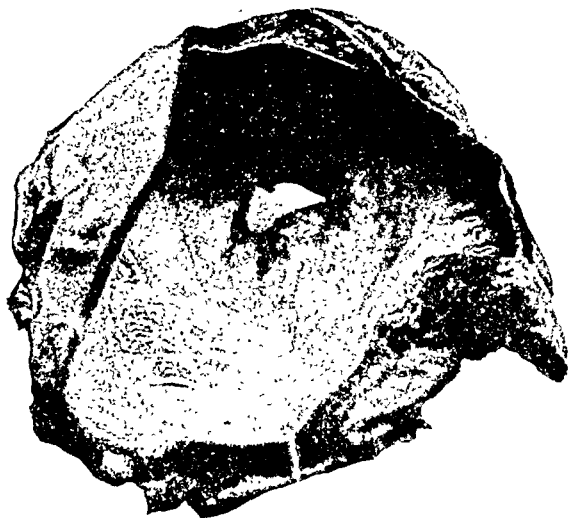


FIG. 1.—High-grade sclerotic involvement of the mitral valve resulting in stenosis and insufficiency.

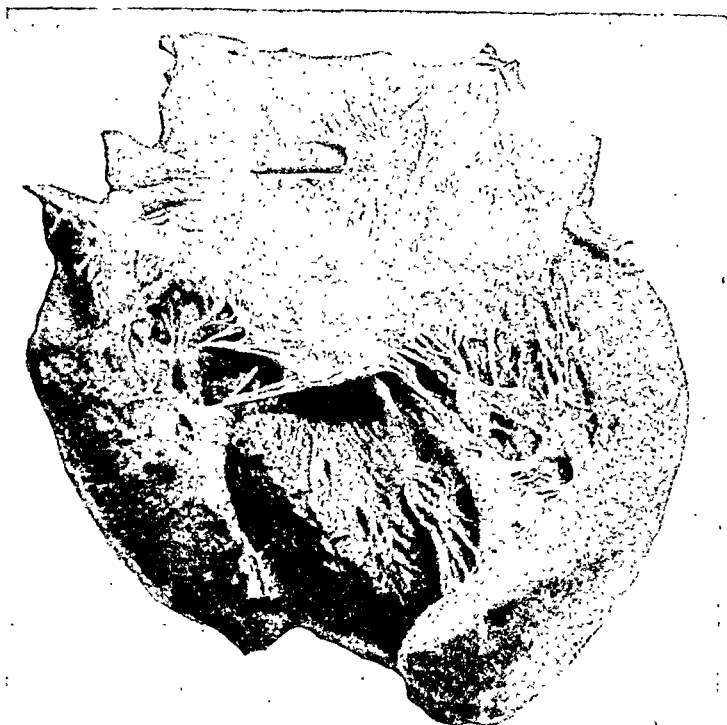


FIG. 2.—Sclerosis and atheroma of the left auricular wall and of the mitral valve.

Microscopic study of the diseased valve leaflets and cusps has shown in the early cases the typical changes of a fibrosclerosis. In more advanced cases atheromatous degeneration is often superimposed, and in a large percentage, lime salts have been deposited, and resulted in a greater or less degree of calcareous change. There has been an entire absence of bacterial findings, and, as far as staining methods are concerned, there has been a complete failure to demonstrate the presence or the causal influence of bacterial forms. I shall later refer to the possibility of the demonstrating spirochetæ in such tissue. The success of a number of laboratory workers in staining the *Spirochæta pallida* in sections of the aorta that have been in preservative fluids for a number of years leads us to believe that we will yet be able to determine a causal organism in at least those instances that depend upon the *Spirochæta pallida* for an etiologic factor. All grades of fibrosis of the mitral valve have been observed from the slightest possible thickening to a gross deformity such as is seen in Fig. 2.

THE PHYSICAL SIGNS AND CLINICAL COURSE OF THE DISEASE. I know no clinical method of distinguishing the sclerotic type of valvular disease from the vegetative except in the probable exclusion of syphilis from the etiology by the Wassermann test. In many of the cases that have come under my observation, syphilis has either been admitted by the patient, or there has been sufficient reason to believe that such an admission would be in order. I believe that many instances of hereditary lues are evidenced in childhood by fibrous arteries and by sclerotic involvement of the myocardium and of the valves—the mitral, the aortic, seldom both in the same case prior to late adult years. I reported several years ago a study of a child of four years dying of a rupture of an aortic aneurysm. The aortic valve was so completely closed by sclerotic thickening and deformity as to cause wonder that enough blood could have passed its ring to maintain life. The child's arteries were of the pipe-stem order. The mother was apparently healthy, but the father had a slight degree of saddle-nose, and developed epileptiform convulsions at thirty-one years. He was in all likelihood a case of latent hereditary syphilis or a none too frank instance of the acquired type.

In a few cases of this nature I have neither been able to obtain an admission from the patient that luetic infection has taken place, nor have I had any reason to think the statement of his freedom from infection was incorrect. I have seen cases that clinically resembled tonsillitis and rheumatism, with endocarditic involvement, which later at the autopsy showed an isolated sclerosis of the mitral valve. I remember one little girl that gave only a history of recurrent tonsillar swelling, yet whose arteries and mitral valve were as rigid as those of an old person.

To the question, What is the exact nature of such a case, I

reply, I do not yet know. Only a searching study of sections of the arteries and the valve leaflets of such cases will exclude the spirochete, and only the Wassermann test, employed as a routine measure in cardiac disease, will assist in the diagnosis *in vivo*.



FIG. 3.—Sclerosis of the mitral valve. Great hypertrophy of the left ventricular wall.

These sclerotic changes occur in the absence of the classical signs of acquired syphilis. Syphilis not infrequently causes a symptom-complex indistinguishable (except by laboratory means) from that of both acute inflammatory rheumatism and of tonsillitis, and it can and does leave in some instances permanent traces in the form of thickening and deformed mitral leaflets. Whether it is the usual cause of these isolated scleroses is another matter. I have also noted two instances of sclerotic involvement of the mitral valve in sisters, members of a family in which a large number of the recent ancestry had been tuberculous. One parent, the mother, had died in early life, probably though not certainly of tuberculosis. The father died of a systemic nervous disease that may easily have been luetic in origin. The children of this parentage, five in number, have all shown evidence of cardiac valvular disease, which in at least two instances was limited to the mitral

valve. Thus we have the possibility of a tuberculous influence and the certainty that syphilis may and sometimes does produce such a picture alone.

Whether other infections may constitute or independently cause isolated valvular sclerosis can only be determined by the studies of many observers of a large series of cases. Dr. James M. Anders informs me that he has studied two interesting cases of this type of mitral involvement in which the causative factor remained unknown. Whether or not acute infectious rheumatism can and ever does cause sclerosis of the valvular tissues is also a point to be considered. As a rule, fibrosis does not form even a prominent feature of the damage consequent upon this disease. Vegetative endocarditis is so generally a rheumatic sequela that this type of valvular disease may almost be regarded as rheumatism of the endocardium. We may therefore pass it over as an unimportant factor in the etiology of the condition under consideration. The text-books have seemingly overlooked mitral sclerosis and implication of the bicuspid valve.

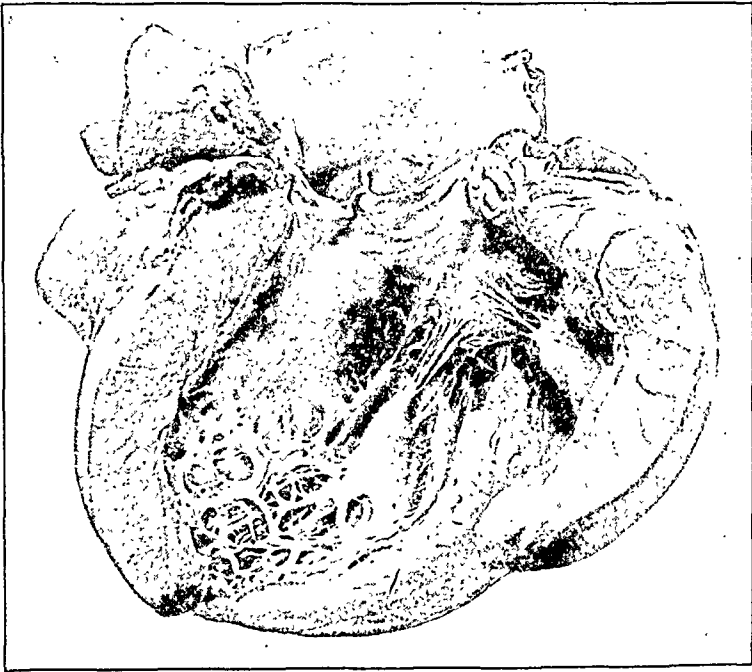


FIG. 4.—Fibrosis of the mitral valve. Marked dilatation of the left ventricle and relative mitral insufficiency. Great hypertrophy of the papillary muscles.

POSSIBILITY OF ANTEMORTEM DIAGNOSIS. From my experience in the cases studied by me I am inclined to believe that all patients, irrespective of age, with sclerosis of the mitral valve, whether associated with other valvular involvements or isolated, will be found also to present sclerotic arteries. The child of four years

already mentioned as dying from a ruptured aortic aneurysm had brachial and radial arteries that would have done credit to an intemperate old man. This early arteriofibrosis, together with a premature overaccentuation of the second aortic sound and a tendency to hypertrophy of the left ventricle, will in the presence of the signs of developing mitral disease afford reason to anticipate fibrosis rather than a deposit of lymph and bacteria as the condition of affairs likely to be revealed at the autopsy. A definite history of syphilis or tuberculosis in the patient or in his or her parents will go far toward rendering presumptive evidence certain.

PREVENTIVE MEASURES AND TREATMENT. The only certain preventive measure would be prevention of marriage among the unfit. The question of the right to marry among those who are morally certain to transmit stigmata, if not actual disease, is not a proper subject for a strictly clinical discussion. It has its bearing, however, immediately we begin to consider the prophylaxis of valvular disease.

I doubt whether in the presence of sclerotic arteries in child or adult much can be done in the way of forestalling sclerotic heart change. Both the cardiac muscle and the valve leaflets seem destined to proceed in the course which they have begun before the presence of a toxic factor has been recognized. It is probably too late for us to expect much valvular benefit from antiluetic medication, though in the presence of repeatedly positive Wassermann reactions, thorough courses of arsenic and mercury should be instituted. The studies of Finger and other reliable investigators would seem to indicate that hereditary syphilis is an incurable disease. In the absence of such symptoms as those of lues, we are peculiarly helpless against the insidious march of an irremediable affection. The treatment therefore again reverts in the present very imperfect state of our knowledge of the etiology of these conditions to a new interest in human eugenics, and to precautionary breeding measures that will prove as intelligent in the reproduction of the human species as in the raising of healthy cattle, horses, and hogs.

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital; assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. I, March, 1913; pp. 353. Philadelphia and New York: Lea & Febiger.

THE first volume of Progressive Medicine for this year opens with an article of 106 pages on the surgery of the head, neck, and thorax by Charles H. Frazier. The hypophysis, meningitis, and trigeminal neuralgia are among the most important subjects considered under the head. A wealth of interesting material is reviewed in the course of his discussion of the thorax, particularly surgery of the heart and great vessels, intratracheal insufflation, and surgery of chronic disease of the lungs. The most noteworthy topics discussed in the remainder of his contribution are cancer of the mouth, lips, tongue, and pharynx, cervical lymphadenitis, cervical ribs, goitre, and breast tumors.

John Ruhräh has contributed a most interesting article of 112 pages on infectious diseases. He lays particular stress upon cerebrospinal fever, diphtheria, kala-azar, leprosy, pneumonia, poliomyelitis, scarlet fever, tetanus, typhoid fever, tuberculosis, and pertussis. No one can read this summary without being impressed by the notable advances that are being made in this branch of medicine.

Diseases of children are considered by Floyd M. Crandall in a short article. After dwelling upon infant mortality and child welfare, he takes up among other subjects, hemorrhage in the newborn, edema in infants, chorea, achondroplasia, the exudative diathesis, and infant foods.

Rhinology and laryngology are ably discussed by George B. Wood. He first reviews the question of the choice of anesthetics for nose and throat operations; then among other interesting topics, he considers submucous resection of the nasal septum, nasal diphtheria, various forms of rhinitis and accessory sinus disease; septic

sore throat and Vincent's angina are among the subjects taken up under the pharynx. He then discusses the tonsils and their surgery, and finally devotes considerable attention to the larynx.

A contribution on otology, by A. B. Duel, completes the volume. He fully enters into the subjects of meningitis, the labyrinth, the treatment of specific disease of the ear with salvarsan, otosclerosis, and neoplasms of the ear.

The volume is one of decided value and the authors are to be commended for their careful selection of so many subjects of great present-day interest.

G. M. P.

APPENDICITIS. By JOHN B. DEAVER, M.D., Sc.D., LL.D., Professor of the Practice of Surgery, University of Pennsylvania. Fourth edition; pp. 379; 14 illustrations. Philadelphia: P. Blakiston's Son & Co., 1913.

SEVENTEEN years ago the first edition of this book was criticised—on the whole unfavorably—by the present writer. The specific counts of the indictment against the book were chiefly as follows: (a) A lack of information as to the proportion of recoveries from genuine attacks, without operation; as to the number of such cases who have second attacks; as to the proportionate fatality of such recurrences as compared with primary outbreaks; as to the relative advantages of immediate operation and of delay in cases seen some days after the primary seizure, and which show signs of the formation of a localized abscess; as to the existence or non-existence of "stercoral typhlitis," and of the "simple catarrhal" or "mechanical" forms of appendicitis, those thought to be caused by a stretching or a twisting of the meso-appendix; (b) insufficient description of the relapsing and recurrent forms of the disease and of its complications; (c) a too free use of other authors without adequate acknowledgment; and (d) a too absolute insistence upon the rule that "where practicable all cases of appendicitis should be operated upon as soon as the diagnosis has been established," though as to the last point, the reviewer added: "This may be good surgery; time will show."

It has been most interesting to read the present edition of this book with these criticisms of nearly two decades ago in mind. It is fair to say:

First, that such retrospective comparison demonstrates that, as has been the case with many reviewers, from the days of "The Dunciad" or of "English Bards and Scotch Reviewers" down to this relatively insignificant instance, it is apparent that it is easier for a reviewer to be, or to seem, clever than to be just. There

were faults to be condemned, of course, but there were also excellences to be commended, and it is now apparent that the latter were not given their proper proportionate prominence.

Second, whatever may have been the genuine faults of the edition of 1896, they have in the changes and additions of the intervening years practically disappeared from the edition of 1913.

The experience and the resulting statistics, not only of the author, but of the whole profession, have so vastly broadened during this period that questions which were then pressing for solution are no longer debatable, and analytical studies of series of individual cases, then much to be desired would now be a waste of time and effort.

The increased experience of the author is shown in the fact that whereas the first edition was based on a "series of 500 cases" his present views have back of them "an experience involving about 10,000 cases of appendicitis" (p. 224).

As to the supposed individual faults of the early edition, we now find by contrast a thorough and entirely satisfactory description of all the varieties of appendicitis and of its complications, clear and succinct, but comprehensive.

Familiarity with the literature of the subject is shown, but the fullest possible credit is given where credit is due. The teachings as to operation are no less positive, but, as to this, it should certainly be admitted that the surgeon who has seen 10,000 cases of a particular condition has at least twenty times the right to be uncompromising or even dogmatic in his advice to practitioners and students that he had when he had seen only 500 cases. In reality, his right to be positive increases far more than by that simple arithmetical proportion. It is certain that when, as in these instances, he speaks clearly and unequivocally, and bases his teachings not only on his own experience, but on well-sustained and well-defined clinical and pathological theories, the professional world must listen respectfully.

Some specific comparisons with the earliest edition may be made with advantage.

The section on Differential Diagnosis contains more than twice the number of words and a vastly more useful comparison of the various conditions that may be confused with appendicitis. Clinical Etiology is similarly enlarged and improved. The section on Pathology, increased more than four-fold, is a masterly exposition of our knowledge of this underlying subject. The summaries of the Principles of Symptomatology (p. 195) and of Diagnosis (p. 216), the Recapitulation of the Pathological Factors (p. 170), the discussion of the Medical Treatment of Appendicitis (p. 355), may be singled out for approval as special examples of the admirable handling of the subject that characterizes the book as a whole.

Particular mention should also be made of the section on Peritonitis, which is exceedingly interesting and instructive. Most surgeons of today will agree with the author when he states (p. 32) that saline enteroclysis by Murphy's continuous method is the greatest advance in the postoperative treatment of abdominal conditions in the last decade. He says that by its use he has been able to reduce his mortality in cases of diffuse peritonitis to less than 2 per cent.—a truly noteworthy showing.

The most radical change of opinion the reviewer has noticed relates to the early administration of laxatives, and it is instructive to note that in 1896 that was a question as to which he and the author were in absolute accord.

In the first edition, Dr. Deaver said: "I am perfectly familiar with the unfavorable opinions of a number of other writers upon the advisability of the administration of laxatives in appendicitis, but my experience has taught me that it forms the only successful, and therefore justifiable, treatment when operation cannot be performed. I do not hesitate, therefore, to offer it to my readers as sound and rational therapeutics. I repeat that laxatives should be given early, and in sufficient quantity to produce thorough evacuation of the bowel, for they accomplish the most good when given thus. . . . The benefit of unloading the bowel far outweighs the danger of breaking up any adhesions that may be forming."

In the present edition he says: "The most important points to be observed in the suspected presence of acute appendicitis are negative rather than positive, and consist in the prohibition of everything by mouth, including water, and especially the avoidance of all purgative medicine."

He also prohibits anodynes, and at present the only difference in our respective views would be that at the end of the above-quoted sentence we would say "especially the avoidance of all anodynes," leaving to purgatives a secondary place as to possible harmfulness. At any rate, this example shows what is apparent throughout the book, that the author has the courage of his convictions and is still young enough to change his mind.

We have noticed but few typographical or other errors. On page 40 the reference to the period when prompt "ablation of the diseased organ meant cure without hope of relapse," should probably read "*fear* of relapse." The latter was scarcely to be "hoped" for by any one. On page 217, the statement that fever is "next to never" the first symptom, sounds a trifle colloquial. On the same page we would prefer to see "excrutiating" spelled "excruciating," though in these days of changing orthography, that is of slight importance. On page 357, "Purgatives . . . hastens," should, of course, take the singular form of the verb. But the proof-reading in the main has been well done and the whole book is

creditable as to its style and manner as well as to its teachings. Indeed, as to the latter, it is not over-praise to say that it is at once the most clear and compact and the most authoritative presentation of its important subject that is today before the medical profession.

J. W. W.

AUGUSTUS CHARLES BERNAYS. A MEMOIR. By THEKLA BERNAYS.
Pp. 309. St. Louis: C. V. Mosby Company, 1912.

THIS memoir of the late Dr. Bernays written, by his devoted sister, constant companion, and chief confidant, has been read with a great deal of interest by the reviewer. The early life of the subject of these pages, treated in the first six chapters, of which chapters there is a brilliant interlude by Prof. Furbinger, were read with the most pleasure. They seemed to be, in a sense, an extremely intimate and therefore affectionate portrayal of the early days of any man, wherein the vagaries of youth and the budding of maturity are all set forth in a way that reminds us of certain pages of "Jean Christophe." We were perplexed to discover what might be the motive of the authoress in offering to the public and to the cold gaze of the reviewer, this scene of family with its manners, trials, successes, affections and love, for such things are generally beheld only by a favored few. This perplexity was unfortunately increased by our lack of familiarity with the work, achievements, or even name of Augustus Charles Bernays. The bibliography appended to the memoir shows the wide scope of his medical writings, and but added to the chagrin of the reviewer in being so lamentably unfamiliar with "one of the most brilliant surgeons that this country has ever produced," to quote from the publisher's letter.

We do not wish to hurt the feelings of a sister who can so lovingly and appealingly record the virtues of an adored brother, and who can so tenderly and with such a gentle way of offering excuse for what she indeed thinks to be the opposite, pen his peccadillos. Miss Bernays' quaint remark on things medical, her naïve comparison between gastrostomy and appendectomy, and her ingenuous chapter on Dr. Bernays' Views on Fever, wherein, unconsciously, she sets forth her own at great length, all these add to the charm if not to the value of the volume. We have gathered the impression, we who have perused carefully, calmly, and dispassionately these memoirs, that they are to be considered as a protest against what the authoress regards as harsh treatment by the medical profession of her brother during his life. The reviewer being unfamiliar with Dr. Bernays' medical activities in St. Louis cannot judge of this treatment, but he believes *De mortuis nil*

nisi bonum. Perhaps the friends, enemies, colleagues, and students of Dr. Bernays will find the book of interest, but to the general medical public it cannot make a lasting appeal unless it does so as the literary product of a mourning sister still crying as she does in her pages, "Never was there another such a brother."

E. H. G.

THE PATHOLOGY OF THE LIVING, AND OTHER ESSAYS. By B. G. A. MOYNIHAN, M.S. (London), F.R.C.S., Honorary Surgeon to Leeds General Infirmary; Professor of Clinical Surgery at the University of Leeds, England. Pp. 260. Philadelphia and London: W. B. Saunders Company.

THIS little volume consists of nine now familiar essays by one of the most noted abdominal surgeons of the world, and should prove a welcome addition to many a medical library. The essays were for the most part originally delivered as addresses before various medical societies, and although dealing with surgical subjects, are of no less interest to the general practitioner than to the surgeon. On the contrary, it is to the general practitioner that they should be recommended particularly, for it is safe to say that if the lessons taught in the essay on Pathology of the Living were firmly fixed in the minds of more general practitioners, more gastric carcinomas would come to the operating table at a period when they are operable, and fewer cases of gastric ulcer would be treated for months as chronic indigestion.

The essays which comprise this book are so well known to the profession at large that they require no detailed comment. It is interesting to note, however, that many of the statements made for the first time by Moynihan in these addresses, all of which were delivered prior to the latter part of 1908, have been amply confirmed by the subsequent investigations not only of Moynihan, but also of a large group of abdominal surgeons in both Europe and America.

G. M. P.

SURGICAL OPERATIONS WITH LOCAL ANESTHESIA. By ARTHUR E. HERTZLER, M.D., Surgeon to the Halstead Hospital and to the Swedish Hospital, Kansas City. Pp. 205; 104 illustrations. New York: Surgery Publishing Co., 1912.

THIS work has been undertaken to supply a demand for a systematic, concise description of the uses and possibilities of local anesthesia. The author has made it a one-man book in that he

gives merely his own technique and ideas. He describes only those operations which he thinks are applicable to local anesthesia.

In discussing the advantages of local over general anesthesia he fails to appreciate the advantages of nitrous oxide and oxygen as a general anesthetic.

The technique is described in minute detail, even including sterilization of skin and the demeanor of the operator. Of the various drugs employed the quinine urea solution is rightly regarded the safest. Cocaine is advised for the operations demanding only small amounts of the anesthetic. Novocaine and eucaine are much favored because of their non-toxicity.

The remaining thirteen of the seventeen chapters are concerned with the description of various operations. Each operation is described fully and individually. The anatomy, neural especially, is outlined, the drugs, amounts used, and technique described step by step in detail. Thus the operator can read up his entire procedure in the one work.

The style and diction of the work are good and make pleasant reading. However, the book has been poorly edited, as typographical errors are noticeable, such as misspelled words and the transposition of parts of sentences.

The illustrations fall short of accuracy in one or two particulars, and consequently would tend to confuse rather than aid the reader.

However, the work is an instructive one in many respects, and one that every surgeon should have at his command.

E. L. E.

ON THE PHYSIOLOGY OF THE SEMICIRCULAR CANALS AND THEIR
RELATION TO SEA SICKNESS. By JOSEPH BYRNE, A.M., M.D.,
LL.B. Pp. 569. New York: J. I. Dougherty, 1912.

As stated in the preface to this volume, its author undertook to write an article on the etiology of seasickness some years ago, but "not satisfied with a mere expression of his view without appeal to experimental fact, and believing that the semicircular canals were in some way involved in the causation of the malady, he undertook a series of experiments, using rotations, aural irrigations, stimulation of the retina by strong light, galvanism applied to the mastoid areas, etc., to determine whether by such means phenomena resembling those of seasickness could be experimentally reproduced."

The text of this elaborate work is divided into three sections: (1) General anatomical and physiological considerations; (II) physiology of the semicircular canals; (III) seasickness. Pp. 339 to 525.

We may dismiss the first part without other comment than it is fully lucid and up to date.

The second part, physiology of the semicircular canals, commences with a summary of the most authoritative results of experimentation on animals, and then details a long series of personal experiments upon human subjects, the results of which are minutely described, as they were manifested in organs near and remote from the aural structures. Numbers of these are tabulated in series of elaborate protocols, any summary of which here would be too superficial for usefulness.

The third part is an equally elaborate experimental study of seasickness and its results on board ship. The general conclusions convinced the author that the effects of real seasickness are quite analogous to the artificial sickness caused by rotation, aural irrigations, and by galvanism applied over the mastoid areas.

While all this work is learned, laborious, and interesting, it is doubtful whether this physical cause of seasickness is the real one.

To conclude, the treatment suggested for seasickness is quite indeterminate and unsatisfactory.

In maritime circles, however, seasickness of landsmen is often immediately cured by the psychic effects of a rope's end or a knock-down blow with the fist.

J. S. C.

THE SURGICAL TREATMENT OF LOCOMOTOR ATAXIA. By L. N. DENSLOW, M.D., Late Professor Genito-urinary Surgery and Venereal Diseases, St. Paul Medical College, Minnesota. Pp. 118. London: Baillière, Tindall & Cox, 1912.

THE purpose of this small volume is to present a new theory as to the cause of locomotor ataxia and a new method of treatment based upon this theory. The theory is as follows: "The dystrophic changes that occur in the neurons of the posterior roots and their connections in tabes are the result of continuous sensory impulses conveyed from some peripheral point to the sensory roots in the cord; that such continuous impulses, kept up, perhaps, for years, exhaust the central nerve substance which having no rest or intermission from such impulses, and having no opportunity for recuperation, finally succumbs." The "peripheral point" from which the "sensory impulses" originate, in the great majority of cases, is an inflamed or constricted portion of the urethra. About half of the book is given up to a discussion of the theory and the other half to a citation of cases treated by the author. The results obtained are at least suggestive but are not conclusive. The greatest need in connection with the theory and treatment is confirmation by other workers in this field.

T. T. T.

HANDBOOK OF MENTAL EXAMINATION METHODS. By SHEPHERD IVORY FRANZ, PH.D., Scientific Director and Psychologist, Government Hospital for the Insane; Professor of Physiology, George Washington University. Pp. 165; 33 illustrations. New York: The Journal of Nervous and Mental Disease Publishing Co., 1912.

THIS small book is one of the Monograph Series published by the *Journal of Nervous and Mental Disease*. The journal deserves a deal of credit for the excellence of its selection, for the series includes translations of such works as those of Sigmund Freud, Plaut, Jung, and others.

The present volume, which is No. 10 of the series, is a manual of the modern methods of examination of mental diseases. It is excellently done, and is a safe guide for those who intend to study psychiatry along modern scientific methods. T. H. W.

THE THERAPY OF SYPHILIS. By PAUL MULZER, M.D., of Berlin. Translated by A. NEWBOLD.

THE *Therapy of Syphilis*, by Dr. Paul Mulzer, consists of a brief essay of 44 pages on the mercurial and the more important arsenical forms of antisyphilitic treatment, other than salvarsan, with a history of their development, shortcomings, and discard; and a rather lengthy treatise of 160 pages on the therapy of syphilis by the Ehrlich-Hata arsenical preparation, dioxydiamidoarsenobenzol or "606."

Mulzer gives a short history of the discovery of "606," and animal experimentation by Ehrlich and Hata, a description of the various methods of preparation of the drug for the different forms of injection, and clinical conclusions on the value, contraindications, criticisms, and results of its use, based on one year's observations (January, 1910 to December, 1910), of many well-known European authorities.

The rapid progress in our knowledge of the handling of this drug, both in the technique of its administration and the clinical discretion in its use, since December 1910, which Mulzer must have foreseen, reflects only credit to his industry in the production of such a work.

This book should be, at least, of historic value and interest to the profession. J. L. L.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Alimentary Galactosuria in Experimental Phosphorus Poisoning.—R. ROUBITSCHKE (*Deutsch. Archiv f. klin. Med.*, 1912, cviii, 225), at the suggestion of Reiss, has studied the galactose tolerance of dogs during phosphorus poisoning. He found that galactosuria occurred with the acute degenerative changes produced in the liver cells. This fact, taken with the results of the studies of Reiss and Jehn, leads Roubitschek to believe that it is only the acute conditions which injure the liver parenchyma diffusely that interfere with the power of the organ to synthesize galactose to glycogen. In chronic conditions such as cirrhosis, chronic passive congestion, etc., there is regeneration of liver cells which may compensate functionally to a sufficient degree to prevent the occurrence of galactosuria.

The Bradycardia of Lead Colic.—It is not uncommon to observe, in the course of lead colic, an outspoken bradycardia. Tanquerel, in an analysis of 1179 cases, has found a pulse of 20 to 60 in 678 instances, 65 to 70 in 376, and 80 to 100 in 125. LION and MARCORELLES (*La Presse Méd.*, 1913, Nr. 12, 109) have applied graphic methods and the atropine test to 4 cases. The tracings proved the condition a true bradycardia, with a normal phlebogram and no auriculoventricular disassociation. Each ventricular systole was preceded by a single auricular systole. The heart was normal but slow. Arterial hypertension and the bradycardia were independent. Both are probably manifestations of saturnine intoxication. In each case, atropine produced a tachycardia, the pulse changing from 46 to 52 to 75 to 120. This leads them to conclude the toxic impregnation is either of the vagus trunk, or the nerve endings in the node of Keith and Flack.

Acetone and Diacetic Acid.—BONNAMOUR and JOUBERT (*La Presse Med.*, 1913, Nr. 14, 130) have modified the Legal and Gerhardt test for acetone bodies in the urine. They emphasize that the two are distinct, the first indicating the presence only of acetone, the second diacetic acid. The Legal reagent as modified was made with 10 grams of glacial acetic acid and 10 c.c. of 10 per cent. sodium nitroprusside. In a colored bottle, this can be kept several months. To 15 c.c. of filtered urine are added 20 drops of reagent. After mixture, ammonia is floated upon the surface drop by drop. The presence of acetone even in dilution of 1 to 2000 causes a violet disk at the line of separation of the two. With the test acetone was detected in the urine of numerous non-diabetic patients. They concluded that acetonuria may be the index of acidosis, but in itself is not an indication of imminent diabetic coma. It is not evidence of the presence of diacetic acid. Gerhardt's test for diacetic acid was performed by adding to urine diluted with four volumes of water a 10 per cent. solution of perchloride of iron drop by drop. Normal urine, containing even acetone, gives a white cloud. In urine with a trace of diacetic acid, the precipitate is a definite black violet cloud. The reaction is much more delicate than the original Gerhardt test, and is given only by diacetic acid. The two reactions are distinct for each acetone body.

Syphilitic Aortitis.—LONGCOPE (*Arch. Int. Med.*, 1913, xi, 15) has observed no definite beneficial effect from salvarsan in 20 cases of syphilitic aortitis. Neither the cardiac competency nor the anatomical condition have been changed. Signs of aortic insufficiency have not been reduced and aneurysms have not grown smaller. The most striking result has been upon the pain and attacks of paroxysmal dyspnea. The relief has been immediate and tends to be permanent. The persistence of a positive Wassermann reaction or the rapid return of a positive reaction after a temporary abatement during treatment have impressed the author. The improvement in symptoms manifests itself very rapidly, usually within four to six days, but this is associated with an increase in the severity of symptoms within twenty-four hours to forty-eight hours after the intravenous injection. This is particularly true of angina pectoris and paroxysmal dyspnea. The rapid amelioration of the pains, attacks of angina pectoris, and paroxysmal dyspnea suggests certain explanations for these symptoms. Autopsies have not been convincing of any direct association between diseases of the coronary arteries and these attacks. The suggestion is strong that the symptoms are associated with the inflammatory reaction at the root of the aorta and directly dependent upon it. The increase in the severity of symptoms after injection resembles a Herxheimer reaction, the increase in symptoms due to increased reaction of the tissues toward the liberation of toxins in excess from rapidly destroyed spirochetes. The dyspnea caused by bronchospasm, and the contraction of the peripheral arteries producing heightened blood pressure from aortic irritation in experimental animals is a close reproduction of the paroxysmal dyspnea, as it occurs in syphilitic aortitis. Longcope believes these symptoms dependent upon a reflex generated at the root of the aorta by the syphilitic inflammatory process. At any rate, the true etiology probably lies in the diseased aorta, and this

is supported by the Herxheimer reaction, combined with the rapid improvement and later recurrences. Longcope in conclusion considers that syphilis produces a characteristic lesion of the aorta which is responsible for most aneurysms, about 75 per cent. of cases of aortic insufficiency in adults, many cases of dilatation of the aorta, and a certain group of cases of angina pectoris. The infection of the aorta probably taken place during the secondary stage, and the process usually remains latent, or unrecognized for an average of sixteen or seventeen years. Thus syphilitic aortitis is probably a common cause for a positive Wassermann reaction in so-called latent syphilis.

Congenital Family Steatorrhea.—GARROD and HURTLEY (*Quarterly Jour. Med.*, 1913, vi, 242) report the case of a boy, aged eight years, subject from infancy to true steatorrhea, the passage from the bowel of liquid fat which solidifies on cooling. His parents are first cousins. A brother was similarly affected from birth. The boy is well nourished and exhibits no other morbid conditions. There are no signs of pancreatic disease besides the steatorrhea. On a diet containing very little fat his stools assume a normal appearance and consistency. Analyses show he excretes in his stools 25 per cent. of the fat taken by mouth. Improved saponification is not followed by improved absorption. The boy is presumably the subject of a rare inborn error of fat absorption, probably a Mendelian recessive characteristic. Investigation did not reveal where the error lay.

On Uric Acid Excretion in Hypophyseal Disease.—W. FALTA and J. NOWACZYNSKI (*Berlin. klin. Woch.*, 1912, xl, 1781) find no data on uric acid excretion in hypophyseal disease. Their own findings on a limited material are of considerable interest. The patients were placed on a purin-free diet, and the uric acid of the urine was determined by the method of Hopkins-Folin-Shaffer. In 3 cases of acromegaly they found the endogenous uric acid to be twice the normal average or greater. In 1 patient there was an endonasal resection of part of the hypophysis. No clinical evidence of improvement was noted shortly after the operation, nor was there any decrease of the uric acid output, compared with the pre-operative periods. In this patient there was a prompt increase in uric acid following the administration of 20 grams of sodium nucleinate. In 2 cases of dystrophia adiposogenitalis associated with hypophyseal tumor (one hypophysis cystic at autopsy, the other "a tumor in the hypophysis region"), they found, on the other hand, that the endogenous uric acid was normal or subnormal, with only a slight response to the administration of sodium nucleinate. They assume that the acromegalics are suffering from an increased functional activity of the hypophysis, and on this basis they suggest that the determination of endogenous uric acid may be of some diagnostic value, provided their results are borne out by the study of a larger material.

Autoserotherapy and Absorption of Ascites.—VITRY and SÉZARY (*Revue de Médecine*, 1913, xxxiii, 86) studied the absorption of ascitic fluid in a case of cirrhosis of the liver. The patient, a woman, aged fifty-two years, had noticed the insidious swelling of the abdomen

for six months. The abdomen was bulging with a large ascites, estimated at 8 to 10 liters. There was a prominent collateral circulation. The cause of the hepatic lesion was obscure, probably alcoholic. On a milk diet, the urinary output was 1000 to 1400 c.c. Subcutaneous injections of ascitic fluid were given; 10 c.c. were injected in the abdominal wall immediately after withdrawal. This was done every two days. On the third day an abundant diuresis began and increased to the point when eleven days later the therapy could not be continued for lack of ascitic fluid. The body weight diminished in a corresponding way. An increased chloride content coincided with the polyuria and loss of weight. The acidity of the urine was diminished by the elimination of the alkaline ascitic fluid. The authors were impressed with the favorable influence, although they claimed no effect upon the condition of the liver. However, the disappearance of evidence of portal obstruction was maintained, even when the patient returned to a salt-containing diet.

On the Presence of Typhoid Bacilli in the Mouth of Typhoid Fever Patients and Typhoid Convalescents.—B. PURJESZ and O. PERL (*Wien. klin. Woch.*, 1912, xxv, 1494) have made cultures from the gums, tonsils, and tongue of patients suffering with typhoid fever. Sterile swabs were rubbed on the mucosa, and then, tubes containing Conradi-Drigalski medium were inoculated. The organisms were finally identified by agglutination tests with the serum of a rabbit inoculated with typhoid bacilli, whose serum agglutinated in a dilution of 1 to 3000 in twenty minutes. They examined 17 cases in all. In about 50 per cent. of the cases a positive result was obtained. During the febrile period a positive culture was obtained as late as the twentieth day. The authors have obtained the organisms from the mouth as late as the fourth to eighth week of convalescence, confirming the observations of Gould and Quales, which appeared during the course of the authors' study. The findings are important both from the standpoint of diagnosis and epidemiology.

Blood Findings in Adiposity.—CARO (*Berlin. klin. Woch.*, 1912, xl, 1881) has made counts and histological studies of the blood in 34 patients suffering with adiposity. There were 19 cases of "constitutional" adiposity, 6 cases following the climacteric, and 9 cases of "alimentary" adiposity. The blood showed constantly a lymphocytosis, as high as 62 per cent., with a decreased percentage of polynuclear neutrophile cells. The total number of leukocytes tended to be high—up to 12,000. The red cell count was frequently slightly reduced. Except for lymphocytosis in 1 case of hypophyseal adiposity and in 2 adipose eunuchs, the author has been unable to find reports of blood examinations in adiposity in the literature. Under the influence of thyroid tablets, the lymphocytosis observed by him decreased or disappeared, and there was a corresponding increase of the neutrophiles, in a few cases in which the gland was administered. Kocher has observed similar blood changes in myxedema after administering thyroid gland—for here, too, in untreated cases there is a lymphocytosis.

SURGERY

 UNDER THE CHARGE OF

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A Procedure for Wide Extirpation of Cancer of the Prostate.—GAYET, CHAMPEL, and FAYOL (*Jour. d'Urolog.*, 1913, iii, 333) say that up to the present time three perineal paths have been employed for the removal of a cancerous prostate. These they designate as the anterior, middle, and posterior. The anterior is through the anterior triangle of the perineum. In the middle, which is more frequently employed, a transverse incision is made between the two tuberosities of the ischium. In the posterior the incision is made from the tuberosity of the ischium to the coccyx. Gayet, Champel, and Fayol utilize the whole length of the perineum, the incision passing well to the left side of the anus. The following is a brief outline of the operation which they describe: The patient is placed in the lateroventral decubitus or the pelvis may be extremely elevated so that the perineum looks toward the ceiling. The incision which passes from the root of the penis to the coccyx is deepened and the rectum separated and pushed posteriorly. The posterior surface of the prostate, the seminal vesicles and the posterior inferior surface of the bladder are then exposed. If the lateroventral position has been employed, this is now changed to the dorsal with extreme elevation of the pelvis. The perineal floor is now divided in its whole length and the rectum is pushed further backward and to the right side. The finger recognizes the apex of the prostate and membranous urethra which is easy if a sound or catheter has been placed in the urethra. The urethra is opened in front of the apex of the prostate and through this opening an elbowed retractor is introduced. The urethra is divided transversely in its whole circumference and the prostate is separated from the surrounding structures by scissors, the hemorrhage being controlled by a gauze tampon. If the prostate can be depressed far enough, a puncture is made by a bistoury through the anterior wall of the bladder above the portion invaded by the tumor. This opening is enlarged on both sides by scissors, giving a wide opening into the bladder. The posterior portion of the bladder in the region of the trigone and ureters is now well exposed. With catheterization of the ureters, the rest of the separation of the prostate and tumor can be completed under the guidance of the eyes. The separation of the divided ends of the urethra and bladder is considerable, but their elasticity aided by a

moderate liberation of the urethra permits them to be brought together by sutures. But it is not necessary to suture them together in their whole circumference, a large opening in the bladder being left posteriorly. Through this opening a large tube is passed and fixed in position with a catgut suture. The muscles of the perineum are then restored very incompletely and a large drain is introduced penetrating to the side of the vesical tube. The skin margins are then brought together, leaving a large median opening for gauze drainage. The results of this operation in two cases were benign. At the end of five weeks in the first patient all urine passed in the natural way and in the second patient more quickly, without the necessity of catheterization or dilatation.

Traumatic Epilepsy after Head Injuries in the Japanese-Russian War.—EGUCHI (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxi, 199) says that head injuries frequently produce traumatic epilepsy. From 1.3 to 4.7 per cent., on the average 3 per cent., of all skull injuries admitted to the reserve hospitals of Japan during the war were followed by traumatic epilepsy. In these, injuries of the bone and dura mater produced irritation of the brain. Wounds of the soft tissues alone gave no cases of epilepsy. The symptoms followed not only injuries of the cortex in the motor area, but many times injuries in other areas. The traumatic epilepsy appears usually after cicatricial tissue develops. Its occurrence at an earlier stage is very rare. It was more frequent after sagittal than after transverse gun-shot wounds. The frequency was in proportion to the size of the brain injury. The autopsy did not show in any case any changes in the medulla, pons, or cerebellum. Scars of the head are very irritable in cases of traumatic epilepsy, and are very tender on palpation. If a bone defect is covered only with a flap of soft tissues, the pulsation of the brain can be seen. The soft tissue flap used corresponded to that of Kocher. Adhesions between the dura or skin and the brain frequently produce epilepsy, as does traumatic new formation, such as thickening of the inner table of the skull, cysts, abscesses, etc. Foreign bodies, pieces of bone, and in war especially, splinters of bone or pieces of missiles, cause epilepsy by pressure on the dura and brain. All of Eguchi's cases developed a nervous disposition. Epilepsy develops easily after head injuries in nervous people. The shortest period from the day of the injury to the beginning of the epilepsy was 3 days, the longest was 442 days, the average 161 days. Medicines, especially the bromides, cannot suppress the attacks before operation, but after operation has been done the attacks, which recur in some cases, can be more quickly controlled by the bromides. Operation gave good results in Eguchi's cases. A cure was obtained in 11 cases, or 90.9 per cent., and no results in 1 case, or 9.1 per cent. The death in this last case was not the result of the operation, but of the bursting of an aneurysm. In all of the other cases no attack had occurred two years after operation. One should operate on all cases of traumatic epilepsy from head injuries in which he detects scars, or wounds, or other changes. If the epilepsy developed a short time before the operation, a quick result should be expected. If the attacks have been occurring for a much longer period, the operation may be followed by several attacks.

Partial convulsions disappear more quickly after operation than general convulsions. In operating, two kinds of flaps may be employed; without a bone defect, like that of Wagner, and with a bone defect covered by a soft tissue flap. Pieces of bone, foreign bodies, and bone thickening should be removed. Adhesions should be separated between the skin and bone, bone and dura, and dura and brain. The dura may be excised. Cysts and abscesses should be incised and scars excised.

Treatment of Spontaneous Gangrene of the Extremities.—KOGA (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxi, 371) says that spontaneous gangrene of the extremities from arteriosclerosis in the young is more common in Japan than in Europe. His chief, Ito, attributed this to the greater use of a vegetable diet in Japan. Until the present time we have been almost powerless to prevent threatening angiosclerotic gangrene, or to restrain it when it develops. The results of arteriovenous anastomosis have not been favorable. In only 8 out of 63 cases collected by Zesas was improvement or a cure obtained. Koga has tested the viscosity of the blood in a series of cases of spontaneous gangrene and found it almost always of much value. Reduction of the increased viscosity by saline infusions influenced the gangrene favorably. The administration of potassium iodide had little or no effect on the gangrene. Koga reports 13 cases, varying in age from twenty-four to forty-eight years. He determined nothing definite as to the etiology, and the urine contained nothing abnormal and particularly no sugar. Syphilis was always excluded, the Wassermann reaction being negative in every case. They were cases of presenile gangrene, in which the viscosity was increased, as a rule, and was reduced to the normal by the saline solution. Simultaneously the symptoms improved, the edematous swelling decreased, as did the cyanosis, and a sharp line of demarcation developed. Ulcers became clean and cicatrized, and the pulsation of the arteries which could not be felt before the introduction of the saline infusion, reappeared. The pain also disappeared so that the patient could sleep, the feeling of cold was not complained of, and the patient could walk a considerable distance. The blood, having its viscosity reduced, gets through the vessels easier and then favors the development of collateral branches. Koga believes that the condition of sclerosis is improved. He reviewed his cases last December, by mail, and found that the improvement or cure had lasted a variable period. In one case amputation had been done for recurrence. In another a black spot had appeared on the same foot. Repeated infusions might have prevented the recurrences. The effect of the infusions on spontaneous gangrene does not appear to be of short duration.

Paralysis of the Phrenic Nerve from the Employment of Kulenkampff's Brachial Plexus Anesthesia.—SEIVERS (*Zentralbl. f. Chir.*, 1913, xl, 338) reports the following experience following the injection of the brachial plexus above the clavicle for anesthetization of the upper extremity. It was done for the treatment of a wound of the soft tissues on the ulnar side of the right hand, in a healthy young man, and 20 c.c. of a 2 per cent. novocain bicarbonate solution was

injected. The anesthesia was sufficient at the end of a quarter of an hour to permit the operation to be completed without further anesthesia, although the radial side of the hand was not completely anesthetized. At the beginning of the treatment of the wound the patient began to complain of severe pain in the right side of the chest, which increased during the operation. The breathing was inhibited as in a dry pleurisy, every deep inspiration being prevented. The Röntgen rays showed at first almost complete arrest of movement in the right half of the diaphragm. Later there was slight movement of this side, but considerably less than on the left side. The condition remained unchanged for several days except that the pain became less, and the disturbances disappeared in about four days. Three explanations are offered for the development of this paralysis of the phrenic nerve: (1) It may have been due to an endoneural injection of the cervical portion of the phrenic; (2) to a subfascial diffusion of the anesthetic fluid to the nerve; (3) or to an extension of the fluid to the apex of the pleura. Seivers favors the third explanation. The apex of the pleura lies just underneath the brachial plexus and a considerable quantity of the anesthetic fluid is injected, so that it could easily extend along the loose connective tissue over the pleura to the phrenic nerve, which passes downward on the anterior and mesial surface of the pleura. This complication is not, however, a contraindication to this method of anesthetizing the upper extremity. It may be serious, however, in affections interfering with the respiratory organs, since the interference with expiration and coughing might lead to retention of the secretions and pneumonia. Kulenkampff called attention to the possibility of a paralysis of the phrenic nerve in the employment of his method of injecting the plexus.

The Extended Abdominal Radical Operation for Cancer of the Uterus.—WEIBEL (*Surg., Gynec., and Obst.*, 1913, xvi, 251) says that in criticizing the value of the operation we should first calculate how many of all cases subjected to the radical abdominal operation are free from recurrence at the end of five years (after results), and then calculate how many of all cases examined in the clinic (including the inoperable ones) are well and free of cancer at the end of five years (absolute percentage of cures). The after results were calculated as follows: 380 cases were operated, 8 of these died from intercurrent diseases, and 160 were well and free of recurrence; therefore, 43 per cent. of all operated cases could be permanently cured. If the primary deaths were left out of the calculation (because they cannot come into consideration with respect to the after results), we have 53 per cent. permanent cures of all cases surviving the operation. Calculating the absolute efficacy he gets the following results: 863 cases with cancer of the cervix were examined in this five-year period, 36 of them refused the proposed operation, and 8 died from intercurrent diseases; from the rest (819) 160 cases were well and free of cancer. It is 19.5 per cent. absolute efficacy, 1 per cent. more than he had in his first 250 cases. With these results we can say that the radical abdominal operation for cancer of the uterus cured permanently a fifth of all these cases examined in the clinic; it cured permanently 43 per cent. of all operated, and 53 per cent. of all cases surviving the operation. In

the last 175 operations he has been able to reduce the primary mortality to 9 per cent. The raising of the operability, the permanent falling of the mortality, and the increasing in the operative technique allow him to hope that he will be able to report much better results in the next years, when his present cases have passed the five-year limit.

THERAPEUTICS

UNDER THE CHARGE OF

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Syphilitic Disease of the Aorta.—DENEKE (*Deutsch. med. Woch.*, 1913, xxxix, 441) believes mercury is a more reliable remedy for the treatment of syphilitic aortitis than salvarsan or neosalvarsan. He advises giving a combination of mercury and iodide when the Wassermann reaction is positive and iodide alone when the reaction is negative. He says that salvarsan should not be given to patients with serious aortitis and great caution is necessary when giving it to patients with the milder forms of aortic disease. He gives salvarsan only in small doses from 0.2 to 0.4 gram, and always with mercury or the iodides. The guide as to the length of treatment is the Wassermann reaction, and this should become permanently negative before treatment is discontinued. This result may never be obtained, but the treatment should be persistent. Temporary improvement often follows antisyphilitic treatment in cases of aortic disease, but permanent results depend upon the thoroughness of the treatment.

Action of Benzol on Leukemia.—KLEIN (*Wien. klin. Woch.*, 1913, xxiv, 357) has treated 22 cases of leukemia with benzol in the past six months. The details of 12 cases are given in the article. He gave the benzol mixed with olive oil either in milk or in a capsule. His average dose was less than 4 grams a day, and he thinks that the results were equally as good as with higher dosage. Doses as high as 5 grams a day were given in a few cases, and it seemed that these higher doses had an injurious action on the red-blood corpuscles. He also injected the benzol subcutaneously in dosage of 1.5 grams once a day, mixed with an equal amount of olive oil. None of his patient showed any signs of irritation on the part of the kidneys. His results were not so uniformly favorable as those reported by Kiralyfi, Koranyi, and others, but he thinks that benzol is a decided aid in the treatment of leukemia. The best results were obtained when the benzol treatment had been preceded by a course of x-ray treatment. He advocates the combination of these treatments in all cases of leukemia, especially for those with a very high leukocyte count. No difference in the effect was noted in the various forms of leukemia.

Treatment of Leukemia with Benzol.—STERN (*Wien. klin. Woch.*, 1913, xxvi, 365) reports a case of leukemia of recent origin treated with benzol. The dose was begun at 3 grams a day in capsules with an equal amount of olive oil and was increased to 6 grams a day. At the end of two months the leukocyte count had diminished from 264,000 to 13,300, and the red-blood cells had increased from 3,500,000 to 5,500,000. The differential count changed as follows: Myelocytes diminished from 44 per cent. to 3 per cent.; polynuclear leukocytes increased from 48 per cent. to 74 per cent. The spleen decreased in size in proportion to the improvement in the blood picture, until at the end of the treatment it was normal in size. The patient's general condition improved, the weight increased, and the result seems to be an apparent cure after two months of benzol treatment. Stern says that of course it is too soon yet to say this is a permanent cure.

Experiences with Neosalvarsan.—LIER (*Wien. klin. Woch.*, 1913, xxvi, 410) draws the following conclusions from his experience with neosalvarsan. Neosalvarsan is especially indicated in those cases in which mercurial treatment leads to severe stomatitis or nephritis. In such cases neosalvarsan can be injected repeatedly without periods of interruption of the treatment as is necessary with mercurial treatment. Neosalvarsan may be given intramuscularly because of its easy solubility in water and neutral reaction. The intramuscular injections are very little or not at all painful and they do not leave areas of infiltration at the site of injection. Lier also believes that neosalvarsan can be used with safety in ambulatory cases. He believes that neosalvarsan gives the best results in primary to tertiary syphilis, but that it is also of value in the infectious wet form of the secondary stage. In the dry form of the secondary stage the action of neosalvarsan is weaker than that of mercury, and in these cases it should be used always in combination with mercury. When neosalvarsan is given in combination with mercury the individual injection should be given at longer intervals. Lier believes that neosalvarsan is often able to effect a true abortive cure in primary syphilis if given in large doses at frequent intervals. He also advises a combined neosalvarsan and mercurial treatment in early metasyphilitic diseases of the nervous system.

The End-results of the Abortive Treatment of Syphilis with Salvarsan.—MÜLLER (*Munch. med. Woch.*, 1913, lx, 408) writes concerning 39 cases of primary syphilis treated during 1910 and 1911 by what he terms the abortive treatment of syphilis. This treatment comprises excision or cauterization of the primary lesion, three intravenous injections of salvarsan of 0.4 gram each, and five injections of 40 per cent. calomel in oil (0.5 to 0.07 gram) and 40 per cent. mercurial 0.1 to 0.14 gram. Nine of these cases disappeared from observation, but in the 30 cases observed up to the present time none has shown any clinical manifestation of the disease, and the Wassermann reaction remains persistently negative.

Cholesterin in Paroxysmal Hemoglobinuria.—PRINGSHEIM (*Med. Klin.*, 1913, ix, 254) tried cholesterin in the treatment of paroxysmal

gemoglobinuria on the ground that cholesterin has been found to have an inhibitory action on hemolysis in test-tube experiments. He found that it did abort the attacks and that when it was discontinued the attacks recurred as before. He gave the remedy by intramuscular injections of 5 c.c. at a dose of a 10 per cent. emulsion of cholesterin. No appreciable changes were observed in the blood during the cholesterin treatment. The remedy did not have any permanent effect, however, for a severe and typical attack occurred a week after discontinuing the cholesterin.

The Treatment of Amebic Dysentery with Subcutaneous Injections of Emetin Hydrochloride.—LYONS (*Jour. Amer. Med. Assoc.*, 1913, lx, 1216) reports 6 cases of amebic dysentery treated by hypodermic injections of emetin hydrochloride, 5 of which recovered promptly. Lyons says that the 1 fatal case should be omitted in judging the treatment, as the patient was beyond hope of cure by any method of treatment. The largest dose used was three-fourths of a grain. The average length of treatment until the stools became normal was nine days for the 5 cases. Lyons says that larger doses may be found more effective. There were no ill effects noted from the use of the remedy. He believes the treatment of amebic disease with emetin rests on an experimental basis. It has been shown that ipecacuanha without emetin has but little effect on ameba in vitro (as well as clinically), while emetin has a most powerful amebicidal action. Granting this, then we may assume that emetin is the active principle of ipecac so far as amebas are concerned, and theoretically should be used in preference to the whole drug in the same manner as we employ quinine for the treatment of malaria in preference to cinchona. According to Rogers a third of a grain of emetin is equivalent to 30 grains of ipecac. The soluble salts of emetin are put up by several pharmaceutical houses. The hydrochloride, to which Lyons experience is limited, is practically non-irritating when used subcutaneously, and in moderate doses causes no nausea, vomiting, or depression. Rogers' largest dose was 3 grains in one day. Allen injected 4 grains at one dose and produced nausea for several hours—the patient vomiting once. Rogers has given the hydrochloride intravenously (1 grain in 5 c.c. of normal saline solution) without any depressing effect on the pulse. To summarize, the advantages of the emetin treatment are briefly: (1) Simplicity and ease of administration of the drug; (2) no vomiting or depression; (3) accurate dosage; (4) rapid absorption and effect; (5) reliability of product against the marked differences in the strength of powdered ipecac from different manufacturers. Lyons says that while no definite conclusions can be drawn from the observations of so small a number of cases, he believes that the results are highly suggestive that in the subcutaneous injections of soluble emetin salts an ideal method has been found of treating amebic disease. Time will soon show whether or not, as Rogers believes, another specific has been found.

Amebic Abscess of Liver Treated Successfully by Emetin.—CHAUFFARD (*Bull. d. l'Acad. d. Médecine*, 1913, lxxvii, 122) reports a case of a large amebic abscess of the liver that after about a year per-

forated into a bronchus. When the emetin treatment was begun the patient had been for five months raising a considerable amount of reddish pus averaging each day from 200 to 250 c.c., and during this time had become emaciated and septic. At the same time there was some ulceration in the rectum. The x -ray examination showed an opacity at the base of the right lung merging with the shadow of the liver. The patient was given six injections of emetin hydrochloride, each 0.04 gram, during a period of five days. The injections were practically painless and produced no local induration. The expectoration was reduced to but a slight amount on the fifth day of the treatment, and after that it stopped entirely. The temperature fell to normal and the leukocyte count dropped from 49,000 to 19,800, and the polynuclear from 77 per cent. to 63 per cent. The ulceration in the rectum healed and subsequent x -ray examinations showed that the base of the right lung had cleared up. The patient improved markedly in general health and increased in weight 13 pounds. Chauffard believes that his experience with the clinical results reported by others demonstrates that emetin is a specific for amebic disease like quinine for malaria.

PEDIATRICS

UNDER THE CHARGE OF

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Chronic Infective Endocarditis.—EDMUND CAUTLEY (*Archiv. of Pediatrics*, 1913, xxx, 328) offers the histories of a number of cases of this kind, with comments on each. This disease is infrequent in older children and young adolescents, is acute in type, and recovery is exceptional. The following cases are in accordance with the established opinion that infective endocarditis is secondary to pre-existent valvular disease and may affect any valve: An instance of the pyemic type affecting the tricuspid valve occurred in a young adult. After three months in the hospital the patient was discharged cured, except for a permanent tricuspid regurgitant murmur. A case, secondary to mitral valvular disease, in a girl, aged sixteen years. Death occurred from rupture of an aneurysm of a cerebral artery caused by an embolus. A case secondary to rheumatic fever and congenital heart disease in a girl, aged fifteen years. Death occurred from recurrent hemoptysis due to emboli carried to the lungs. A case affecting the aortic valves, probably secondary to a previous heart condition in a boy, aged eight years. Death occurred from meningitis in eleven days, probably from infection carried from the heart. Death results more commonly from secondary effects such as cardiac failure or infarction rather than from toxemia. This is illustrated by two cases. One case of chronic infective endocarditis of the pulmonary valve in a child, aged eight years, was in the hospital eight months. Death was caused

by thrombosis of the pulmonary artery, caused partially by prolonged toxemia and wasting. Fever and wasting were constant and prolonged. The spleen was much enlarged. A reduction in fever occurred with the onset of edema and ascites. Serum and vaccines were valueless. The other case was in a boy, aged eighteen years, in whom the tricuspid and aortic valves were involved. Death was due to a terminal infection of the lower lobe of the left lung and secondary cardiac failure. The spleen was much enlarged but the degree of fever less than in the first case. A streptococcus was found in the blood but autogenous vaccines were useless and the streptococcus was probably due to the terminal infection. Serum and vaccine treatment are practically hopeless, except they may in some cases enable the body to destroy the infective agent if given very early. Quinine, arsenic, iron, and perchloride of mercury are of value.

Diphtheritic Paralysis.—J. D. ROLLESTON (*Archiv. of Pediatrics*, 1913, xxx, 335) reports his findings in a study of 2300 cases of diphtheria with especial reference to diphtheritic paralysis. He found it exceptional for paralysis to develop after the sixth week. Of the 2300 cases, 20.7 per cent. showed some form of paralysis. In each series of 100 cases the percentage of paralysis was never less than 10 or more than 31. He shows that there exists a close relation between the acute attack and the subsequent paralysis. The more severe the acute attack the more frequent and severe the subsequent paralysis. Where the nostrils as well as the throat are affected the incidence of paralysis is greater than when the fauces alone are affected. Pure nasal or laryngeal cases showed practically no subsequent paralysis. Affection of the tendon jerks and the presence of Babinski's sign is more common in severe than in mild attacks. But 1.3 per cent. of the cases showed a relapse and none of these cases developed paralysis. Second attacks, varying from three months to fourteen years, were found in 2.1 per cent. of the cases. Paralysis was more frequent in children than in adults, the majority occurring between two and six years of age. Early injection of antitoxin undoubtedly jugulates the disease, and minimizes the occurrence of complications. Cardiac and palatal paralyses are the only ones occurring during the first fortnight. After this time no serious palsy occurs, as a rule, until the fifth week. During the fifth and sixth weeks other palsies develop, such as ocular, diaphragmatic, etc. In this series 85 deaths were due to paralysis. The prognosis is better in older patients. There was no fatal case above the age of thirteen years. Cardiac, pharyngeal, and diaphragmatic palsies are the only kind which may cause anxiety. A well-marked serum reaction at the usual period after injection is a favorable omen. It is exceptional for cardiac paralysis to be fatal in these cases. In severe cases the patients should not be allowed to sit up for six weeks.

Summer Heat and Summer Diarrhea.—HECTOR CHARLES CAMERON (*British Jour. Child. Dis.*, 1913, x, 205) believes that this subject has been dealt with too exclusively from the point of view of the epidemiologist. All factors in the etiology of summer diarrhea other than microbic contamination have been too much neglected. Even if we could secure a faultless supply of milk we should still

witness an enormous rise in the frequency of diarrhea as a symptom during hot weather. Heat may have a direct effect on the infant, increasing the amount of summer diarrhea. The increase may be due to indirect effect of the heat by lowering the tolerance to food, by increasing the danger of overfeeding in a thirsty infant, by lowering the immunity of the child to infections, and by aggravating the course of all alimentary and infectious disorders of whatever nature. Heat may exert an indirect effect by favoring the multiplication of micro-organisms without the body. If the cause of summer diarrhea is to be found in the multiplication of bacteria in milk, then some explanation must be found for the frequency with which breast-fed infants are attacked and for the high mortality among babies fed on condensed milk and patent foods, in which the bacterial content is relatively low. A vast amount of bacteriological work has not succeeded in establishing a causal relation between any one organism and so-called epidemic diarrhea. In the rise in incidence of summer diarrhea all the factors mentioned have a part, and of all deaths registered as due to diarrhea in the summer, a small fraction only is due to bacterial infection of the alimentary tract. Greater emphasis should be laid on prophylactic measures such as an adequate quantity of water, reduction in carbohydrate food, cooling baths, light, porous clothing, and proper ventilation.

OBSTETRICS

UNDER THE CHARGE OF

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Albuminuria Likely to Recur in Successive Pregnancies.—Under this title SLEMONS (*Amer. Jour. of Obstet.*, May, 1913) discusses the question of prognosis in cases which have suffered from albuminuria and toxemia in the first pregnancy. From clinical records it appears that but one in six patients who have had this complication in their first pregnancy may expect its recurrence in subsequent parturition. Lapage (*Annali di ginecologia d'Obstet.*, 1912, p. 577) and Williams, arrive at practically the same conclusion, as among hospital cases 21 per cent. suffered a recurrence of albuminuria and toxemia after the first pregnancy. In the effort to distinguish between those patients who are likely to have danger and those who are not, the clinical course of the two types of auto-intoxication must be studied. A severe attack of scarlet fever in childhood greatly influences the prognosis. Severe toxemia tends to recur in successive pregnancies with increased virulence, and more early in the course of gestation. Where repeated toxemia terminates fatally the kidneys are usually found to be involved. It is sometimes possible to base a prognosis upon the convalescence

of the mother from the first auto-intoxication. If this is prolonged and imperfect, the outlook for the future is correspondingly bad. Slemons would classify cases of albuminuria with toxic symptoms in the later months of pregnancy into three groups; two are well defined and likely to suffer from recurrence, while the third will almost certainly be exempt. He has not found the nitrogen partition to be useful in reaching a prognosis, but he believes that the estimation of the quantity of albumin is helpful. The greater it is and the longer it persists, the more extensively are the kidneys damaged. In cases where the liver seems especially involved and the kidneys normal, the prognosis as to recurrence is good. Blood pressure is more satisfactory than albumin as an index, and upon this basis cases may be divided into three groups. In nephritic toxemia a pressure of 250 m.m. is frequently observed. In toxemia it is at its height; the pressure was rarely below 180 m.m. In cases studied from this basis, 75 per cent. of patients having eclampsia are not likely to do so again; while in 15 per cent. extensive lesions of the kidneys made the prognosis bad; 10 per cent. of toxemic cases are uncertain as to prognosis. Chemical methods in estimating the efficiency of the kidneys have proved disappointing. Slemons concludes that at present we have no better clinical methods for deciding the nature of a toxemia and of reaching an ultimate prognosis in the study of the albumin and blood pressure during convalescence. In nine out of ten cases a satisfactory conclusion can be reached from this data, and auto-intoxication does not return in approximately 80 per cent. of cases.

Abderhalden's Serum Test for Pregnancy.—BEHNE (*Zentralbl. f. Gynäk.*, 1913, No. 17) has tried Abderhalden's method of dialysis in the diagnosis of pregnancy in the clinic at Kiel. His observations in 44 cases show that this test gives regularly a positive result in normal pregnancy. In advanced gestation, in some cases the results are negative. Patients who are not pregnant but who suffer from an inflammatory condition of the genital organs, with the production of pus or with suppuration in some other portion of the body, as in the breast, often give a positive reaction. In the differential diagnosis between ectopic gestation and inflammatory conditions of the adnexa, the test by dialysis does not give a definite differential diagnosis. Positive reactions are obtained with serum in pulmonary tuberculosis and diseases of the liver.

Puerperal Eclampsia.—GIBBONS (*British Med. Jour.*, April 26, 1913) reviews to a considerable extent the literature of the subject and states that we know of nothing which can definitely be described as the cause of the disease, although all evidence goes to show that it is a poison circulating in the blood. Rapid emptying of the uterus by the most safe method available, after the first few convulsions, seems to give the best prognosis. The greater the delay the greater will be the danger to the mother.

Unusual Fertility in Syphilitic Patients, with Anomalous Involvement of the Child.—WATSON (*British Med. Jour.*, April 26, 1913) reports the remarkable instance of the family of a wandering gypsy,

the mother of the family having brought one of her children for examination. Multiple dactylitis was present, of syphilitic origin. On examination, the mother was aged twenty-one years, well nourished, and gave a negative history, believing that she had never had venereal disease. On examination, there was a scar on the right labium. She had three times given birth to twins, without miscarriages. All of the children were born prematurely, the first pair at the seventh month, and the others at the eighth month. The first twins were normal in size, the others smaller. The father had undoubtedly had syphilis, and was fairly vigorous, but was mentally deficient and seemed to be in the very early stage of general paralysis of the insane. The first twins seemed in perfect health and showed no evidence of syphilis. The second pair had thickening in the bones and dactylitis, and the parents stated that the children had eruptions on the buttocks when they were six weeks old. The third twins had a condylomas, sore eyes, and peeling of the skin of the hands and feet. There were also marked snuffles and a coppery eruption on the nates. The serum of the parents and children in each case gave a very positive result. This family of gypsies were wandering about the country subsisting merely by selling tin cooking utensils which they made. They are a source of danger from infection and such individuals should be segregated to prevent the danger of spreading syphilis in the community.

The Condition of the Blood Serum of Mother and Fetus in the Pyelitis of Pregnancy.—WEIVEL (*Archiv f. Gynäk.*, 1913, cxix, No. 2) has studied the question of the formation of antibodies in the blood serum of mother and fetus in cases where pregnancy was complicated by pyelitis. He finds that the colon bacillus passing from the intestine into the urinary tract takes up its new functions and activities from the antibodies, and what he styles the third order may be detected in these cases; the reactions are not always typical, and the organisms having immunity show in various cases great differences, which complicate the results of clinical and bacteriological examination. When antibodies were found in the serum of the mother, they were also present in the serum of her child or children. In some cases they were also present in the amniotic liquid in a greatly lessened quantity. In the serum of the fetus these bodies disappeared shortly after birth. It is evidently not yet practical to employ this reaction in making a diagnosis of infection by the colon bacillus.

Subcutaneous Symphysiotomy.—KEHRER (*Archiv f. Gynäk.*, 1913, cxix, No. 2) reports 10 cases of subcutaneous symphysiotomy, which he performs under ether or chloroform anesthesia, or in some cases by spinal anesthesia. Under antiseptic precautions two fingers of the left hand are inserted in the vagina and the urethra carried to one side. The clitoris and meatus are pushed, so far as possible, out of the way, and an incision made directly with the scalpel upon the middle of the symphysis. The under portion of the symphysis is separated through two-thirds of the joint. The edge of the knife is then turned upward and the upper portion of the joint severed, while the separation is made complete in the surrounding tissues by the

use of a smaller scalpel. When the ligamentum arcuatum is severed the pubic bones separate, and the legs of the patient are rotated outward and somewhat inward by assistants, to prevent the laceration of tissue. The wound is then packed with gauze and the extremities closed with metal clips. The bladder is then carefully emptied completely by catheter, and the patient placed in bed, when pituitrin in some form is given by intramuscular injection. The upper portion of the patient's body is slightly raised, the knees are brought together, the thighs bandaged, and the knees slightly separated as birth occurs. After the birth of the placenta a permanent catheter is placed in the bladder for several days. In 118 cases the maternal mortality was 0.8 of 1 per cent., in comparison with 4.1 per cent. in 217 subcutaneous hebostiotomies. There was no fetal mortality. There is almost no hemorrhage in the operation, the wound through the skin is exceedingly small, and the danger of wounding the surrounding tissues is very slight. In 60 per cent. of cases there was some injury to the crura of the clitoris, and hematoma formed; and in 30 per cent. of the cases thrombophlebitis complicated the puerperal period. No case of embolism was observed. The operation finds an especial field in multiparæ, and the best results are obtained when the child is expelled spontaneously. If possible, delivery by operation should be avoided, and some preparation of pituitrin, with possibly Walcher's position, should be utilized for delivery. Uterine inertia is no contraindication to the operation, and it may be performed in pelvis whose true conjugate is as low as 6.9 to 6.8 cm. If care is exercised in delivery and in separating the pelvis, the sacro-iliac joints may not be damaged, and a separation of the pubic bones greater than 3 cm. should not occur. The operation is indicated where cases are suspected of infection. The patients walk well after the operation, and infection does not occur more often than in other cases. The joints unite as well as does the pelvis after pubiotomy, and the pelvis remains somewhat enlarged after the operation. No callus forms, as after hebostiotomy, and the permanent scar is very small. The one essential objection to the operation is the tendency for hematomas to form in tissues about the severed ends of the joint.

GYNECOLOGY

UNDER THE CHARGE OF
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Intestinal Obstruction Due to Retroverted Uterus.—A case of acute intestinal obstruction due to the sudden incarceration of a loop of intestine behind a non-adherent, retroverted uterus is reported by LEFÈVRE (*Jour. de Méd. de Bordeaux*, 1913, xliii, 183). The patient had had for some years a markedly retroverted uterus, which, however,

gave only slight symptoms, until one day, when riding in a carriage, she received a severe jolt, following which she was instantly seized with violent abdominal pain. This continued, and soon vomiting came on, which later became fecal. Nothing was passed by the bowel for forty-eight hours, by which time the patient was in a critical condition, presenting all the classical symptoms of intestinal obstruction. Laparotomy revealed a collapsed cecum and large intestine, but the small intestine was enormously distended up to a point where a loop dipped down into Douglas' pouch behind the uterus; beyond this it also was collapsed. Gentle traction was sufficient to bring the intestinal loop out of the small pelvis, when there was an immediate passage of gas and fecal matter into the collapsed portion of the gut, and the condition was relieved. The patient made an uneventful recovery. Lefèvre believes that at the moment the patient received the jolt in the carriage the uterus was bounced forward for a moment out of its position of extreme retroversion, giving a loop of intestine the chance to slip down behind it. This was then caught by the uterus dropping back against the sacrum, and as distention began to take place behind the point of impingement, intra-abdominal pressure was increased, and the caught loop of intestine still further compressed. The uterus was not pregnant, and was only slightly larger than normal.

Prognostic Value of Leukocyte Count in Pelvic Suppurations.—

A statistical study of 100 cases of suppurative conditions in the pelvis from Hunter Robb's service in Cleveland has been made by J. T. SMITH (*Surg., Gynec., and Obst.*, 1913, xvi, 403) to determine if the pre-operative leukocyte count is of any value in forecasting the outcome of the case. Of course, in cases where the leukocytosis, fever, and other symptoms more or less correspond, that is, with high leukocyte count and high fever, or with low count and slight fever, this point is not of especial significance, but it does furnish us, Smith thinks, with valuable data in that group of cases in which the blood count and temperature record are at variance, that is, in patients with a high leukocytosis (over 14,000) and moderate fever (below 101°), or conversely, with a low count (below 14,000) and high fever (above 101°). In these instances Smith thinks the blood count is of more prognostic value than the temperature, since the recorded results in the 100 cases studied show that some trouble arose in a majority of the cases of pus in the pelvis with a leukocytosis of above 14,000, whereas only a small proportion of similar cases with a count below 14,000 developed any postoperative complications; moreover, the mortality in the first group was 8 per cent., as opposed to zero per cent. in the second.

Callous Ulcer of the Bladder.—BUERGER (*Med. Record*, 1913, lxxxiii, 657) says that within the past two years he has seen 2 women suffering with intense vesical tenesmus, dysuria, great frequency and urgency of micturition, and pyuria, in whom the cystoscope revealed the cause of the trouble to be a solitary, callous ulcer of the trigone, a condition as to whose occurrence doubt has been expressed by a number of prominent urologists. In one of these cases fulguration was tried, but entirely without success, and the author believes that where the

process is deep-seated, has lasted for a long time, with the formation of phosphatic incrustations on the surface, neither the application of silver nitrate nor cauterization will have any beneficial effect. The symptoms are so intense as to demand in every case radical measures for their relief, and Buerger has devised a method of treatment which in the two reported cases was followed by excellent results. He introduces through the operating cystoscope a pair of flexible "punch-forceps" with cup-shaped jaws, directing them against the lesion in much the same way as an ureteral catheter. In each case the entire ulcer was excised by means of these forceps at one sitting, cutting well down into the underlying bladder wall; this procedure was followed by immediate amelioration of the symptoms, the condition rapidly progressing to complete cure. Subsequent cystoscopic examination showed that perfect healing of the ulcer had taken place with complete restoration of the vesical mucosa. Pathological examination of the tissue removed showed a superficial deposit of urinary salts, then a layer of necrosis and ulceration, and beneath this newly-formed connective tissue with active evidences of inflammation.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF
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Three Fatal Cases of Pneumococcal Infection of the Throat.—TWEEDIE (*Jour. Laryn., Rhinol., and Otol.*, April, 1913) places on record the details of a clinical condition which he had not otherwise seen, the mortality of which in his hands had been 100 per cent. Two patients represented the asthenic, and a third the sthenic type of the disease, the latter running a comparatively rapid course from its commencement up to the end. All three were characterized by their absolute lack of response to every kind of general or local treatment employed; and no cause or connection could be ascertained apart from the presence of the pneumococcus in the throat which was present in large numbers in pure culture on the swabs or sputa. There was no apparent ulceration of, nor membranous deposit on the mucous membrane concerned, which was, however, intensely injected and edematous at the commencement of the illness. The main focus of the local lesion in each case appeared to the naked eye as an indolent, necrotic, more or less localized, sloughing area quite distinct from any pathological state usually associated with the term "abscess." Up to the last few days of the disease there was no impairment of the appetite or malaise corresponding with the progressive weakness, raised temperature, or severity of the disease generally.

Abnormal Epistaphylian Tonsil.—DAPITOLO reports (*Annales des Maladies de l'Oreille, du Larynx, du Nez et du Pharynx*, March 3, 1913) a case in a child, aged seven years, upon whom he performed a bilateral palatine tonsillectomy with adenectomy. Three months afterward he removed, with a cold snare, a tumor of the size and form of a large molar tooth inserted by a short pedicle, upon the superior surface of the soft palate. Histological examination showed that it was composed of lymphoid tissue, and Dapitolo believes that it was an adenoid hypertrophy, provoked by irritation from the operation.

A Case of Mixed Tumor of the Soft Palate.—ALAGNA (*Annales des Maladies de l'Oreille, du Lar., du Nez et du Phar.*, March 3, 1913) reports a man, aged fifty-five years, who had a voluminous tumor of the soft palate, with troubles in deglutition and nasal respiration. Histological examination showed that it was composed of a lipomyxomatous tissue, the adipose cells of which were constituted by a mixture of ethers, glycerin, and cholesterine.

Perforation of the Nasal Septum Due to Topical Action of Cocaine.—CHEVALIER (*Revue Hebd. de Lar., d'Otol. et de Rhinol.*, April 26, 1913) presents a thesis on the subject of perforation of the septum due to the sniffing of cocaine which he has frequently observed in individuals who might be classed among degenerates, or who have lost their equilibrium. He has also noticed it very frequently among morphomaniacs. This perforation is always localized upon a point of the septum corresponding with the cartilaginous skeleton, the quadrangular cartilage alone being involved in the necrosis. As to its etiology, the author contends that the leukocytes are killed by the cocaine and become harder, and thus they clog and gradually obliterate the lumen of the capillaries, rendering definitive a local anemia which is originally produced temporarily. This anemia long kept up proceeds to a suppression of nutrition and to the mortification of the tissues which ultimately terminates in the necrosis. An eschar is produced, and its elimination is the first stage in the evolution of an ulceration.

Chondrosarcoma of Nasal Passages.—MR. HERBERT TILLEY (*Jour. Laryn., Rhinol., and Otol.*, April, 1913) presented to the Laryngological Section of the Royal Society of Medicine two remarkable photographs of a young lady of sixteen, with recurrence within a few weeks after recovery from a primary operation, and a second recurrence after a second operation for involvement of the nasal septum and right ethmoidal regions.

Bronchial Asthma Cured by Operations in Rhinopharyngeal Respiratory Tract.—GOGOMANN (*Annales des Maladies de l'Oreille, du Lar., du Nez et du Phar.*, January, 1913) reports the case of a man, aged thirty-five years, a subject of asthma. After destruction of a nasal synechia and of a deviation of the septum, the paroxysms of asthma were arrested; and they disappeared completely after ablation of tonsils containing caseous accumulations in the crypts.

Topical Anesthesia in Sinus Operations.—In a discussion on the technique of operations for perinasal sinusitis, SIEBENMANN (*Annales des Maladies de l'Oreille, du Lar., du Nez et du Pharynx*, January, 1913) affirmed that local anesthesia predisposes to local suppuration, and impedes cure by first intention. Ritter reported that he had had a case of death seven hours after an operation as a result of anesthesia by morphine-scopolamin injection.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Chlorinated Lime in Sanitation.—Chlorinated lime or bleaching powder, popularly miscalled "chloride of lime," is a very remarkable substance which is being used very widely, especially for the disinfection of drinking-water supplies. The subject is summed up in a book entitled *Chloride of Lime in Sanitation*, by ALBERT H. HOOKER (John Wiley & Sons, 1913). Ballard, in 1835, found chlorinated lime to be composed of: Calcium hypochlorate, $\text{Ca}(\text{OCl})_2$; calcium chloride, CaCl_2 ; calcium hydroxide, $\text{Ca}(\text{OH})_2$. Subsequent investigations by Olding and other chemists have shown that calcium chloride and calcium hypochlorite do not exist as such in dry bleaching powder, but are found on dissolving it in water. Calcium oxychloride, CaOCl_2 , is generally accepted to be the essential constituent of dry chlorinated lime, and calcium hypochlorite to be the active principle of the solution. It is also now well understood that chlorinated lime in its industrial application of bleaching, deodorizing, or disinfecting does not act by its chlorine, but by its oxygen. The chemical action is not "chlorination" but "oxidation." Hypochlorous acid (HOCl) is probably the most powerful oxidizing agent known to chemists, and is readily broken up into hydrochloric acid, and liberates nascent oxygen with extreme readiness. Hooker gives convenient methods for making standard solutions of chlorinated lime, with useful tables, comparing parts per million with grains per gallon, expressed in terms of bleach and in terms of available chlorine. As a practical process the use of chlorinated lime for the disinfection of water dates from 1908, when Mr. G. A. Johnson was called to remedy some serious trouble in the water purification at the Chicago stock yards. Filtration of the water of Bubbly Creek was not satisfactory, and Mr. Johnson substituted chlorinated lime for the copper sulphate which had been used. Chlorinated lime is now used by many municipalities to render their public water supply safe. In some places it is used in

conjunction with alum coagulation and sedimentation or slow sand filtration; in fact, it may be used either alone or as an accessory to other methods. Following is a partial list of cities now using hypochlorite of lime in their drinking water supplies: New York, 16 pounds per million gallons; Omaha, $7\frac{1}{2}$ pounds per million gallons after coagulation and sedimentation; Cincinnati, 5 to $12\frac{1}{2}$ pounds—typhoid rate reduced to 5.7; St. Louis; Minneapolis, after mechanical filtration; Toronto, 6 pounds; Montreal, 5 to $7\frac{1}{2}$ pounds; Cleveland, 16 pounds; Erie, 7 to 10 pounds; Chicago; Milwaukee, 6 pounds; Pittsburgh, 3 pounds, after slow sand filtration; Jersey City, 5 to 8 pounds; Council Bluffs, 15 pounds, following alum precipitation; Brainerd, Minn.; Ridgeway, N. J.; Corning, N. Y.; Nashville, Tenn., 14 pounds; Grand Rapids, Mich.; Little Falls, N. J.; Harrisburg, Pa.; Baltimore, Md.; Niagara Falls; Toronto; Ottumwa, Iowa, and others. It is important to remember that in waters treated with chlorinated lime, free chlorine never is present. While the chlorinated lime kills bacteria in the amounts used, it does not purify organic matter, cure discoloration, turbidity, or neutralize tastes and odors in the water. The remarkable germicidal power of chlorinated lime is better understood when it is known that three grains of a practically harmless substance will kill myriads of bacteria contained in a barrel of water. Ordinarily the amounts used are from one to two or five parts per million parts of water. Much more is required in sewage. A bacterial reduction of 99 per cent. may be obtained in a water containing little organic matter, with one part per million, whereas it requires 1 part to 25,000 parts of sewage to affect a similar bacterial reduction. In practice, the average amount of bleach used in water purification is from 5 to 12 pounds per million gallons of water. The bleach cannot be detected by the sense of taste, provided the amount does not exceed 25 pounds. While the chlorinated lime treatment of water supplies is essentially simple, yet it requires able professional supervision else disappointing results will come from haphazard work. The great essential is a uniform dosing of a standard solution. Bleaching powder is also used in the disinfection of the water of swimming pools, for street sprinkling, and flushing, for the disinfection of feces and sputum; and to a certain extent, for the disinfection of glassware, fabrics, brushes, and combs. It is one of the best substances we have for the general disinfection of rough places, such as slaughter-houses, bake-houses, dairies, outhouses, cellars, and the like. In surgery chlorinated soda is used, the action of which is entirely analogous to chlorinated lime.

The Stable Fly as a Carrier of Disease.—SCHUBERG and KUHN (*Arbeiten a. d. Kaiserl. Ges.-Amt.*, 1912, xl, No. 2) have studied the question of the transmission of various infections, particularly relapsing fever, anthrax, Southwest African horse sickness (*Pferdesterbe*), and epithelioma of fowls (*Hühnerpocken*) through the agency of the stable fly (*Stomoxys calcitrans*). The first report of these studies was published a year ago (*Arbeiten a. d. Kaiserl. Ges.-Amt.*, 1911, xxxi, No. 2) with special reference to trypanosomes and spirochetes. The successful results obtained by Schuberg and Kuhn now have an added significance in view of the recent findings which incriminate the stable

fly as a transmitter of the virus of poliomyelitis (Rosenau, Brues, Richardson, *et. al.*, confirmed by Anderson and Frost). Schuberg and Kuhn successfully transferred the *Spirochaeta obermeieri* from infected rats to healthy rats through the bites of *Stomoxys calcitrans*. Practically every one of the flies were able to transfer the infection provided only five minutes intervene between the bites of the infected and the healthy animal. If ten minutes intervene some of the flies are no longer infective, and if fifteen minutes intervene the number of infective flies is markedly diminished. It developed, as a result of ten experiments, that infection did not occur after an interval of thirty minutes. Nattan-Larrier, in 1911, showed that the spirochetæ of relapsing fever may live in the intestinal tract of the ordinary house fly that has fed upon infectious material, and pointed out the possibility of thus transferring the infection. Prior to Nattan-Larrier's work Sergent and Foley showed that house flies (*Musca domestica*) which fed upon the blood coming from the nose of the patient, contained numerous spirochetes which remained intact to microscopic examination at least twenty-four hours. Experiments designed to transfer the infection from man to apes by means of the common house fly were negative. (Other insects, such as body lice, have been incriminated as carriers of the infection of relapsing fever.) Copeman, Howlett, and Merriman, in 1911, showed by coloring flies that they may fly 1700 yards from the place where they are born. It was also shown that a fly may travel about one-fourth of a mile in half an hour. It is therefore evident that a fly such as *Stomoxys calcitrans*, which is strong upon the wing, may convey the infection of relapsing fever for a distance of about 750 feet during the fifteen minutes it remains infective. The experimental investigations upon Southwest African horse sickness (*Pferdesterbe*) were likewise successful in that this infection was transmitted through the bites of the stable fly. Schuberg and Kuhn are careful to note that stall infection is possible, and are in some doubt as to how much of a role the *Stomoxys* plays in nature. These same authors made three experiments by interrupting the bites of *Stomoxys* in epithelioma of fowls (*Hühnerpocken*). All three experiments were positive. Schuberg and Kuhn express the opinion that, in view of the great resistance of this virus, especially against drying, and further, in view of the small amount necessary to reproduce the disease, it is not unlikely that *Stomoxys* may remain infective a long period of time, and it therefore seems that this may be of practical importance in the transmission of the disease in nature. The *Stomoxys* breeds in manure, and it would, therefore, have ready access to chickens, which they are known to bite under natural conditions. Finally, Schuberg and Kuhn succeeded in transferring anthrax to mice and guinea-pigs through the bites of *Stomoxys calcitrans*. These experiments consisted in permitting the flies to feed upon the livers and spleens of infected animals, and the longest interval between such feeding and the bites of the susceptible animal was two hours and ten minutes. In one case successful infection was obtained by the bite of one single fly at an interval of ten minutes. Six experiments were then undertaken to transfer the infection from animal to animal with one positive result. The donor was a mouse having large numbers of anthrax bacilli in its blood at the time of the bite; the recipient was a guinea-pig which was bitten ten minutes

later. It is known that anthrax bacilli appear in the circulating blood suddenly, and in nature flies may obtain the infection in this way or from shed blood. The latter perhaps would be more dangerous on account of spore formation. It is evident that *Stomoxys* cannot play the major role in the transfer of anthrax in nature, but doubtless is responsible for occasional cases, especially anthrax of the skin. Man, as well as animals, may thus receive the infection.

The Role of the Stable Fly in the Transmission of Surra.—MITZMAIN, M. B. (*Philippine Journal of Science*, December, 1912, vii, 6 p. 475) reports the results of a long series of carefully conducted experiments to determine the role of *Stomoxys calcitrans* in the transmission of *Trypanosoma evansi*. Negative results were obtained in attempts at direct mechanical transmission of surra with flies, which were induced to bite healthy animals at intervals ranging from five minutes to three days, after being permitted to complete the feeding upon infected animals. Thousands of *Stomoxys calcitrans* were employed in twenty-nine experiments, involving the use of three horses six monkeys, and twenty-two guinea-pigs. Attempts also proved negative to transmit surra by the interrupted method of feeding. In these experiments the intervals between feeding on infected and healthy animals averaged twenty-five to forty seconds. The only positive result obtained was produced from a succession of 206 interrupted bites, in which the flies were transferred immediately from the infected to the "clean" animal. The flies were applied thirty-two hours during a period of six days. Mitzmain concludes that these experiments indicate that *Trypanosoma evansi* does not develop in the body of *Stomoxys calcitrans*. He was unable to find the organisms of surra in the flies beyond eighteen hours after feeding on an infected animal, and the limit for infection by inoculation was six hours. Pathogenic trypanosomes were found in the proboscis of the fly thirty seconds after feeding on infected blood. However, after one minute and thirty seconds the organisms were not present in the mouth parts in a form capable of infecting by inoculation into guinea-pigs. Mitzmain also found as a result of these experiments, that the wounds made by *Stomoxys calcitrans* are not suitable channels for infection. No evidence was obtained to indicate that *Trypanosoma evansi* is hereditarily transmitted to the offspring of *Stomoxys calcitrans*. The larva of this fly fed on surra blood does not continue to harbor the trypanosoma, and the fly is "clean" upon reaching maturity. Mitzmain believes the the individual glass-tube method is the most suitable for applying flies in feeding on experimental animals, and for keeping flies for long periods under laboratory conditions.

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ORIGINAL ARTICLES

EXPERIENCES WITH STEINMANN'S NAIL-EXTENSION METHOD
IN FRACTURES OF THE FEMUR.¹

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THE essential part of Steinmann's² method consists of a nail which transfixes the soft parts and bone, and which is the sole point of attachment for suitable traction upon the lower fragment. In other words, the bone and soft parts are transfixed by a drill which is left in place with both its ends projecting.

APPARATUS. The steel nail is $3\frac{1}{2}$ mm. thick, 18 to 20 cm. (7 to 8 inches) long; the ends should project $2\frac{1}{2}$ to 3 cm. beyond the skin (Fig. 1). The nail may be driven through the bone either by a simple handle resembling a clock key, or by a bit and brace, or by a geared hand drill (Fig. 2). An adjustable pair of tongs (Fig. 3), the limbs of which are joined by a suitable thumbscrew, forms the most convenient means of attaching extension apparatus to the nail ends.

In describing the typical procedure, let us take, for example, the treatment of a fracture of the femoral shaft at its middle third. The sterilized nail and drilling mechanism are fitted together and placed in readiness. The entire limb is brought close to the margin of the table or bed, so as to prevent interference with the drilling that is to follow. One assistant grasps the patient's ankle and, maintaining traction, elevates the leg, while the operator who is "sterile" applies full-strength tincture of iodine to the skin and does the necessary draping. The leg is then lowered, so that

¹ Read before the Surgical Section of the New York Academy of Medicine, January 3, 1913.

² Nagel extension der Knoche brüche, *Neue Deutsche Chirurgie*, 1912, Band i; *British Med. Jour.*, November 30, 1912, p. 1235.

ankle and knee are close to the edge of the table. Another assistant having sterilized himself, assumes management of the broken limb. The anesthesia (gas) is now started. The assistant steadies the limb (outer margin of the foot must stay vertical), at the same time pulling the skin of the thigh upward. The point of the nail is inserted horizontally and at right angles to the shaft *a finger's-breadth above the upper margin of the external condyle*. As soon

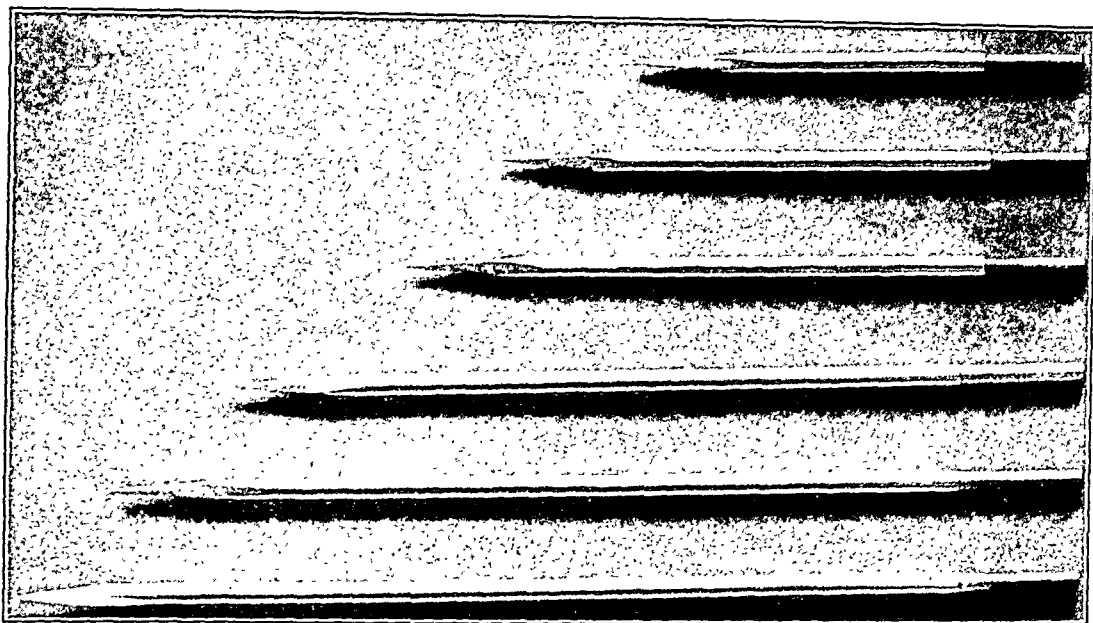


FIG. 1.—Solid nails of varying lengths. The points are sharpened on four sides; the heads are round in order to fit the chuck of the hand drill.

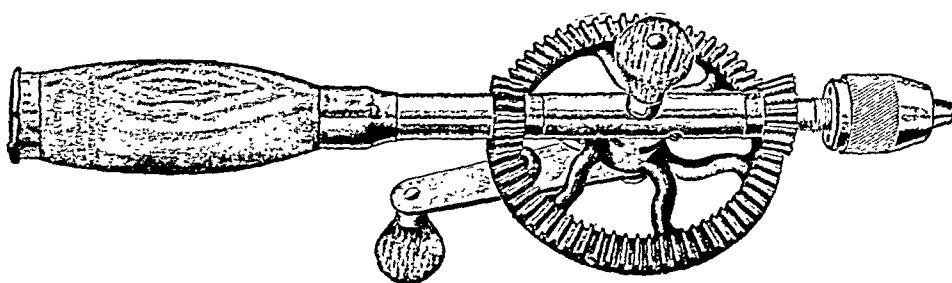


FIG. 2.—Geared hand drill.

as the bone is touched, drilling is begun (Fig. 4). The operator controls the drill with both hands and leans his body, either chest or groin, against the breast-piece of the drill. The resistance which at first is encountered, lessens after a while, for penetration is easier after the corticalis is passed, as the cancellous tissue offers less resistance. Again, progress is slower as the corticalis of the opposite side is encountered. Finally, this also is passed and

the nail point may be felt emerging from the bone. The skin overlying the nail point is pulled upward by the assistant and the

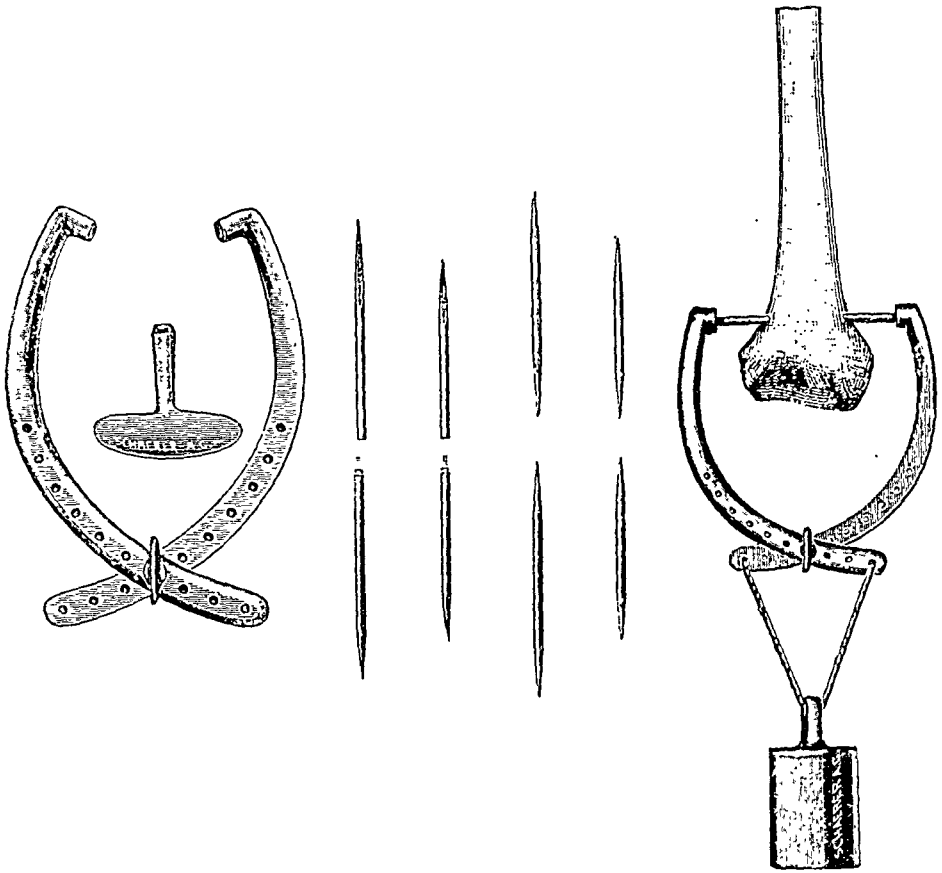


FIG. 3.—Tongs with nails, solid and two piece, and handle.

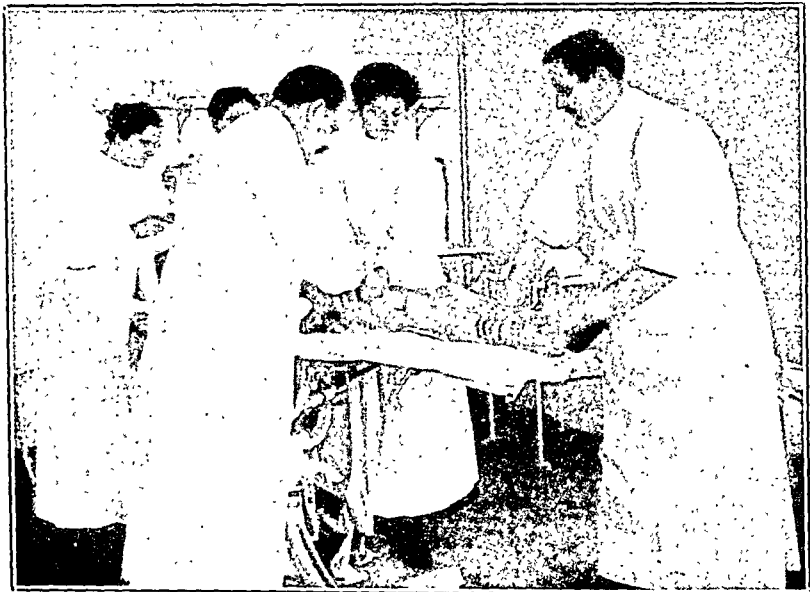


FIG. 4.—Transfixing the lower end of the femur. (Steinmann.)

point finally emerges. Drilling is stopped when the two nail ends project equally on either side of the limb. The narcosis is then stopped. The skin which the penetrating nail point has carried away from the leg is now pushed back on the nail to the level of the adjacent skin. Tincture of iodine, then aristol, and lastly collodion are applied to the skin where the nail emerges. Small flat pieces of folded gauze are transfixd by the nail points and run down the nail shaft to the skin.³ A figure-of-eight bandage holds them in place; it is well for some turns of the bandage to be transfixd by the nail points.

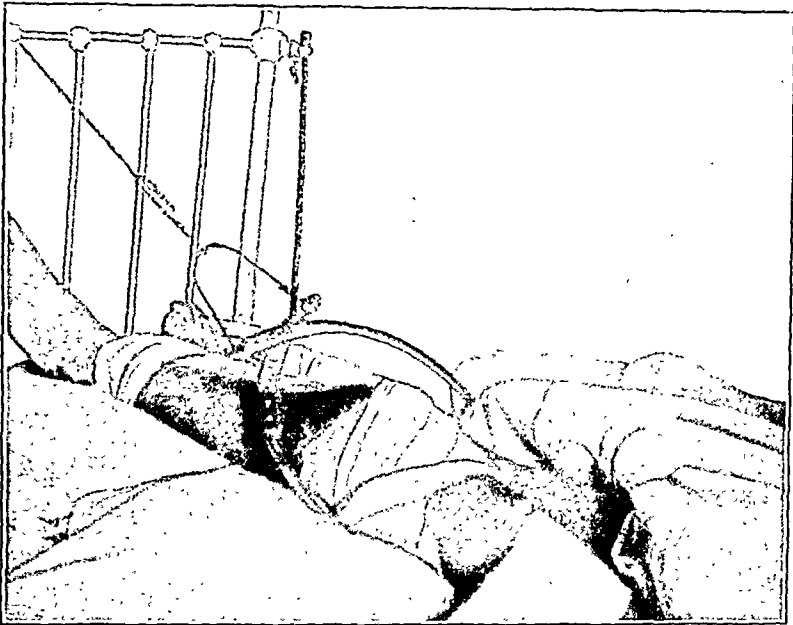


FIG. 5.—Case VI. Nail in supracondylar position. Note wire fastened to ends of crossed limbs.

The extension apparatus is now attached to the nail. The two limbs of the tongs are applied so that the thumbscrew holding them comes uppermost—each limb is applied separately—the screw being inserted in that hole of either limb which most readily falls in alignment. The ends of a short piece of wire are fastened through the outermost holes of the crossed limbs of the tongs (Fig. 5). At the centre of this wire is attached the main traction wire or rope leading over a pulley at the foot of the bed down to the suspended weights. The thigh is placed in semiflexion. The leg is horizontal or the foot may be lower than the knee. The heel should not touch the bed. Hard pillows, sandbags, or suitable splints may be employed to maintain this position. The pulley

³ Another nail may be used to make holes in the gauze, so that it readily slips over the rounded head of the nail which is in place.

at the foot of the bed must be placed so that the wire leading from the tongs is in line with the axis of the semiflexed thigh (Fig. 6).

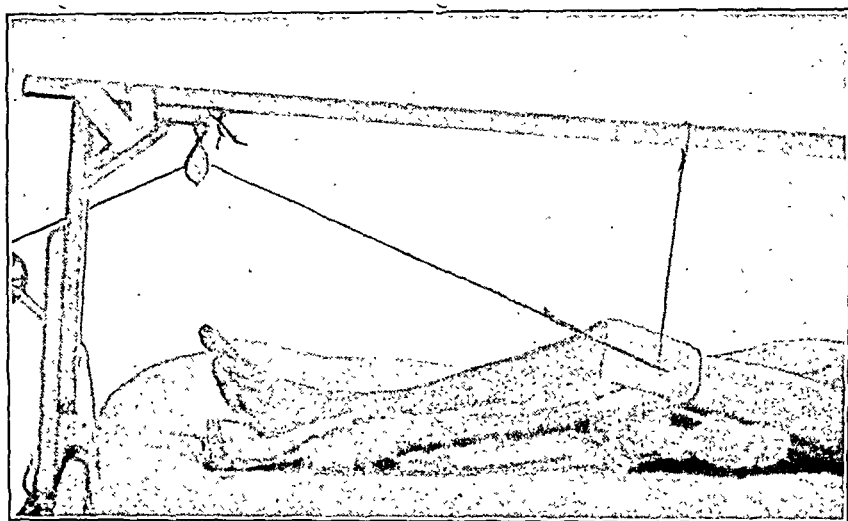


Fig. 6.—Case V. Note traction wire in line with axis of thigh, also suspension of outer end of nail to prevent eversion (rotary displacement).

Naturally the amount of weight to be used depends upon the individual case. In a recent fracture of an adult femur, with 5 cm. shortening, 18 to 20 pounds are usually adequate. It is very convenient to use a small spring scales registering up to 40 pounds, to ascertain how much weight is being applied (Fig. 7).

Countertraction may be obtained by (a) raising the foot of the bed; (b) a well-padded perineal loop attached to the head of the bed, and (c) a foot-rest for the sound limb.

Shortening is usually overcome within a week. The broken limb should be allowed to stretch 1 cm. longer than its fellow. This renders proper approximation of the fragments easier. In transverse fractures, after proper reduction, overcorrection is no longer necessary, while in oblique fractures it is well to maintain $\frac{1}{2}$ or 1 cm. overcorrection until union takes place.⁴ After the shortening has been overcome, less weight is required to maintain the fragments in proper position. Undue lengthening is readily corrected by simply lessening the weight—the limb promptly shortens. Massage and passive motion may be begun five days after nail-extension

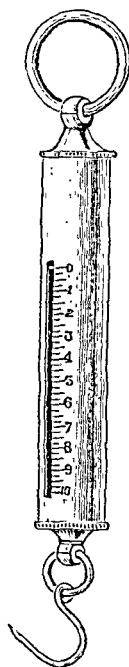


Fig. 7.—Scales.

⁴According to the painstaking investigations of Wettstein (Beitr. z. klin. Chir., 1908, Band ix, Heft 3, p. 684, and Korrespondenzbl. f. Schweizer Aärzte, 1909, No. 3, p. 73) fractured limbs shortened $\frac{1}{2}$ to 1 cm. within the year after union had occurred. To counteract this we institute overcorrection in oblique fractures.

has been instituted. A good callus is usually developed by the end of three weeks. Steinmann states that, if possible, nail-extension should not be maintained longer than three weeks, and never longer than five weeks. Thirty-four days is the longest time I have personally seen the nail-extension maintained.

At the end of three or four weeks there is usually sufficient callus to justify removal of the nail. If the nail is solid the end which is to be drawn through is exposed, it and the adjacent skin are carefully cleansed with tincture of iodine, which is applied most thoroughly, after this the nail is withdrawn. The rounded head is firmly grasped by a heavy pair of wire pliers. The nail is first *rotated* to loosen it and is then extracted with a rotary motion. The knee should be steadied by an assistant. Under gas the actual extraction takes less than one minute. If the nail is in two pieces, the two halves are unscrewed and pulled out, each on its own side. Some tincture of iodine is injected into the nail holes and a wet dressing is applied until the skin is healed, usually within five or six days.

Most of my cases ran a slightly elevated temperature, between 99° and 100°, while the nail was in place; this dropped again upon removal of the nail. There were no signs of infection.

The subsequent treatment is that appropriate for any limb with a fresh callus—namely, avoidance of too much strain on the callus, at the same time employment of suitable passive and active motion.

I. DETAILS OF TREATMENT. A. *Location of the Nail.* According to Steinmann (1) it should avoid the hematoma at the site of fracture; (2) it should avoid the marrow cavity;⁵ (3) it should avoid the joint capsule; and (4) it should avoid the epiphyseal line. Hence the nail is inserted one finger's breadth above the upper margin of the femoral condyle just behind the middle line of the bone—in other words, through the posterior half of the supra-condylar region just anterior to the adductor tubercle or its corresponding site externally.

In fractures of the lower third of the femur the nail is inserted through the upper end of the tibia $2\frac{1}{2}$ fingers' breadth below the upper margin of the tibia on a level with the lower margin of the head of the fibula (Fig. 8).

B. *Methods of Inserting the Nail.* (1) Hammering has been found to cause too much pain at the site of fracture—the risk of splintering the bone is not great.⁶ (2) Boring by hand is safer than

⁵ At the point where the nail passes through the bone, there is enough cancellous tissue to prevent direct communication with the main marrow cavity.

⁶ In a recent case of Dr. William H. Bishop's it was impossible to insert the nail by hand drilling because of the extreme hardness of the femur. The patient was a woman, aged fifty years, with a fracture of the upper third of the bone. A hammer was not available at the time, so the attempt to insert the nail had to be given up. At the subsequent plating the bone was found to be just as hard at the site of fracture, as it was near the condyles. The corticalis was very thick and there was cancellous tissue in the marrow cavity.

by electricity. (3) Incision of the soft parts is unnecessary and increases the likelihood of infection. Other modifications of the method, such as boring a hole and then inserting the nail, etc., can be placed in the same category. (4) It is necessary to pull the skin proximally, especially in supracondylar insertion of the nail, because if this is not done, as the limb is stretched, decubitus of the skin will occur to the distal side of the nail.

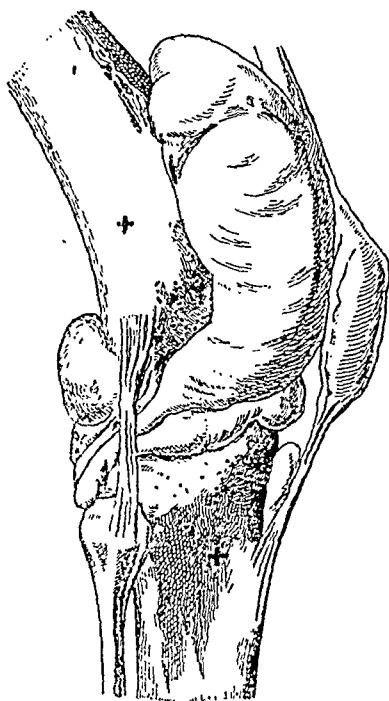


FIG. 8.—Positions for insertion of nails through femur and tibia.

C. *Type of Nail.* The two-piece nail apparently cannot be made of sufficient strength to afford a proper factor of safety against breakage at its joint. The nail has broken six out of the sixteen times I have used it. The weights used were never more than 20 pounds, usually about 15 pounds. Fortunately, when the tongs were used the broken nails were held in sufficiently good position to still maintain traction (Fig. 37). Breaking has occurred during insertion, during transport of the patient in bed to the x-ray room, and with the patient lying quietly in bed as late as the eighteenth day. I therefore prefer solid nails. Both head and point of the original nails are squared. They do not accurately fit the ordinary hand drill with a three-point contact chuck, hence I use nails with round heads which fit the usual types of drill (Fig. 2).

D. *Dressing.* Dressing should be dry and rather voluminous. The details have already been given.

E. *Attachment of Traction.* The tongs are most convenient for this purpose, but they are not essential. Braided picture wire, copper wire, or bandages (Figs. 9 and 14), may be used. In this case the ends of the nail are protected by corks. Spreaders may be necessary to prevent undue pressure of the wire against the skin in some instances, while in others an S-hook or wire loop may be required to prevent the end of the traction wire from slipping off a nail end. Where tongs are used the traction should be made upon the ends of the crossed limbs, not at the point where they cross (Fig. 6).

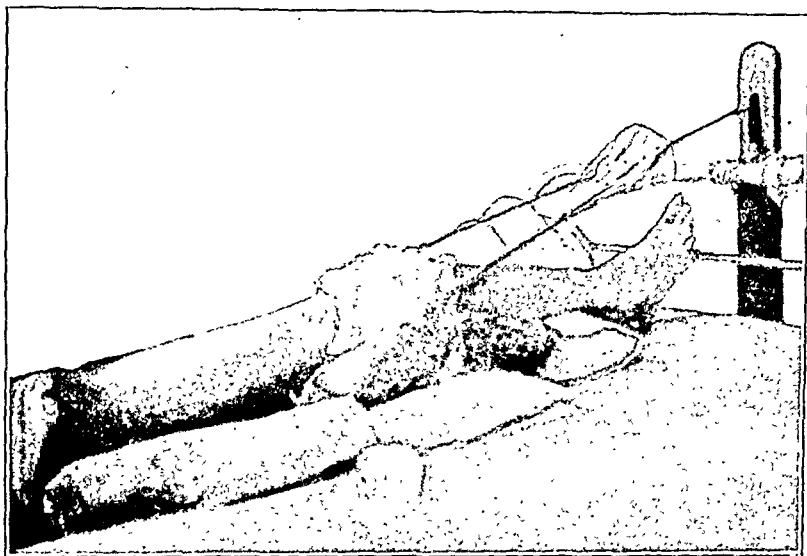


FIG. 9.—Case II. Pertrochanteric fracture. Tongs were not available, so bandages were fastened to the nail ends. Note small sandbag parallel to limb which supports the outer end of nail, thus preventing eversion.

F. *Anesthesia.* There may be a short general anesthesia, either laughing-gas or "aether rausch," or, there may be a local anesthesia (0.5 per cent. cocaine) in the cases where the former is contra-indicated. In intelligent adults it is possible to do without an anesthetic, for the pain of the boring is by no means unbearable (see Case VII). Indeed, most of the pain felt is at the site of fracture.

G. *Amount of Weight.* In recent fractures this varies between 10 and 30 pounds; in old fractures between 20 and 60 pounds. Steinmann speaks of one case where an old fracture with malunion was refractured, nail-extension was applied, and a lengthening of 11 cm. was obtained within eight days. As said before, most of the stretching is done in the first week, after which much less weight suffices to maintain proper position.

H. *Control of Fragments.* The direction of the pull can be varied to adapt the lower to the upper fragment. Strong traction often

causes the upper fragment to follow the lower to a great extent—that is, lateral dislocation is corrected largely by extension alone (see Case VI).

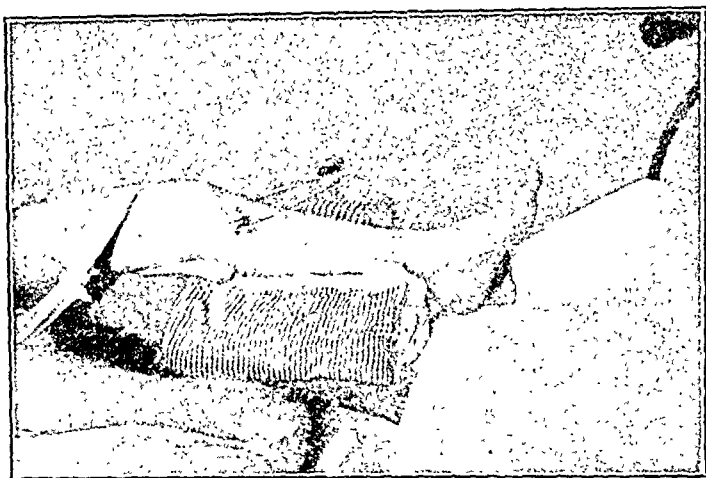


FIG. 10.—Nail-extension applied to head of tibia. (Steinmann.)

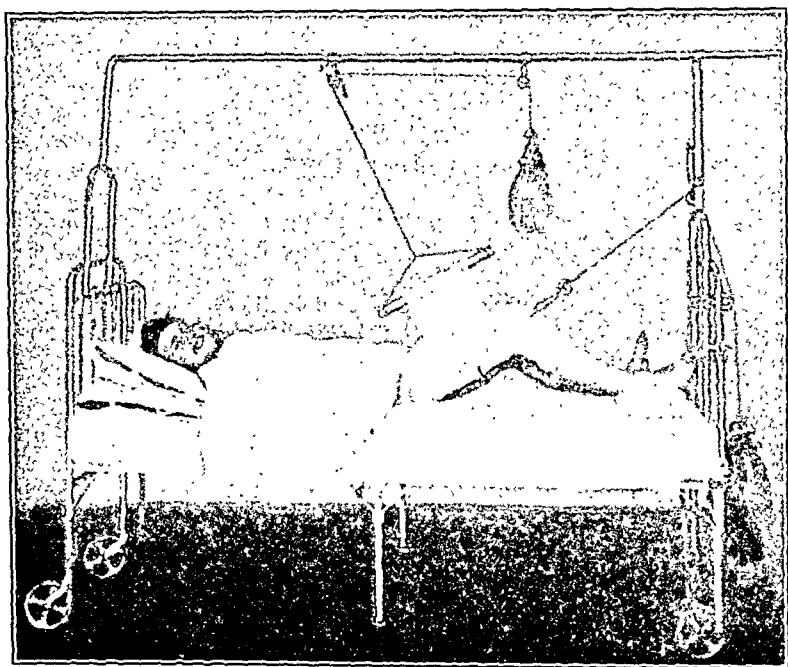


FIG. 11.—Nail-extension, with anterior pull at right angles to limb. (Waegner.)

Posterior dislocation of the lower fragment in supracondylar fractures is known to be especially difficult of correction. Flexion of the leg upon the thigh and dorsal flexion of the foot upon the leg lessens the pull of the gastrocnemii upon the lower femoral fragment which is displaced backward. Traction at right angles to the leg also aids in correction of this condition (Figs. 10 and 11).

Rotary displacement (eversion) is best corrected by suspension of one nail end. This is most conveniently accomplished by two uprights and a horizontal bar running the length of the bed, with a wire attached to the lateral (outer) end of the nail and to the horizontal bar (Fig. 7). In fact, the entire limb may be most conveniently suspended by this simple means.

It is unnecessary to review all the modifications and varieties of lateral traction and suspension which have been employed in other extension methods, notably in that of Bardenheuer. It goes without saying that they have been employed in the Steinmann method since 1907 with even better chances of success.

If possible, *x-ray* plates should be made before extension is applied; afterward controls can be made at proper intervals to make sure of proper position. As a matter of course the exposures should be made both from in front and from the side. Portable *x-ray* outfits are becoming quite common. With one of these exposures can be made without disturbing the limb. In hospitals without portable *x-ray* apparatus, a bed-truck may be used to transport the patient in bed into the *x-ray* room. A physician should accompany the patient upon this journey. The personal supervision of transport by one who understands the *rationale* of the apparatus will prevent unnecessary pain to the patient and undue strain upon the apparatus. As said elsewhere, jarring by rather light weights (15 pounds) during transport has been sufficient to break the two-piece nail at the joint.

Even when the *x-rays* are not available, very fair results can be obtained by careful daily control with tape measure and fingers. While measurement is being made, the sound limb must be flexed to the same degree as the fractured one. It is well to measure from a number of points for the sake of control, for example, from the anterior spine to the nail, as well as to the internal malleolus.

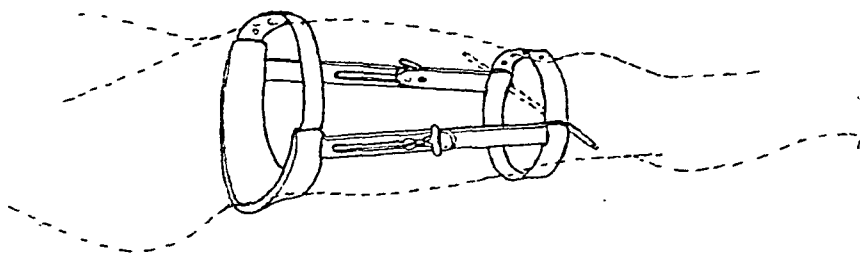


FIG. 12.—Splint for maintaining extension during transport to the *x-ray* room. (Steinmann.)

Steinmann has devised a sort of hip splint which can be adjusted so that its upper margin rests against the pelvis, and its lower margin impinges upon the projecting nail ends; it thus prevents shortening when traction is taken off. This splint was designed to facilitate the transport of patients to some place where an *x-ray*

exposure can be made (Fig. 12). From what I have seen, the less a patient is moved after extension is once applied, the better.

II. OBJECTIONS WHICH HAVE BEEN MADE REGARDING STEINMANN'S METHOD. A. *Pain*. (1) Upon introduction of the nail an anesthetic is usually employed, yet under unusual circumstances it may be dispensed with (see Case VII). (2) During extension no pain is felt at the site of the nail. If traction is irksome the weights may be lessened for a few hours and then added again. (3) At removal of the nail there may be slight pain. By this time the nail is loose in the bone except when lodged in the head of the tibia, from which its extraction may require considerable force. It is well not to allow children or excitable adults to know that a nail is being employed. As long as they are ignorant of its presence they do not complain. A voluminous dressing applied to the leg satisfactorily conceals things.

B. *Infection* occurs either at the time of insertion or after two or three weeks. It is easy to insert the nail aseptically, but it is difficult to keep the region aseptic in the later stages. The granulations which have formed by the end of three weeks afford a fairly good protection to the bone at large. Small local infections have been known to occur, especially in long-continued cases of extension. These have all remained localized. Small circular sequestræ have come away. A small exostosis occasionally develops at the site of the nail. So far there has been no mortality from nail-extension—carried out according to the rules laid down by Steinmann. Fatal cases are known where the wound made by the nail has established communication with the fracture hematoma, thus converting a simple into a compound fracture.

C. *Injury by the nail to important nervous, vascular or articular structures*. There has been none at the time of insertion. Steinmann even reports a case where the nail had been run through the ankle-joint without causing any functional trouble.

The epiphysis has not been harmed, as shown by four years' observations upon children on whom this method had been employed. There was no lessened growth of the injured side.

D. *Injury by too great traction* has been ascribed to nail extension. There has been no instance of harm to the soft parts. An extreme example of what can be accomplished is shown by the case of Steinmann's, where 11 cm. lengthening was obtained within seven days in a refractured malunion of five or six months' standing. There was no loss of function.

E. *Lax Knee-joint*. Strong diversity of opinion exists regarding injury to the knee-joint by traction (such as Buck's extension) applied to the limb below the knee. Naturally this controversy will promptly transfer itself to application of the Steinmann method in fractures of the lower third of the thigh where the nail is inserted through the head of the tibia; hence, a brief outline of the situation seems proper here.

Certain observers emphatically state that they have observed the most harmful effect upon the knee-joint from extension applied to the leg below the knee. Other equally competent authorities maintain that they have never seen any injury to the knee-joint from application of Buck's extension to the leg as well as the thigh, and furthermore insist that no adequate extension can be obtained by merely pulling on the skin of the thigh.

It is to be noted that Steinmann's method differs from Buck's extension in that the knee-joint is flexed, whereas in Buck's extension the knee-joint is fully extended. Perhaps there is less strain upon the ligaments when traction is applied to the partially flexed joint than when there is full extension. My own experience in this matter is not sufficiently extensive to be of much value. Steinmann states that he has never seen any distraction of the knee-joint from traction upon the tibia. He also states that effusions into the joint disappear with great rapidity after extension is made; this likewise has been my own experience. The transient inability fully to extend the knee rapidly disappears under appropriate massage and passive motion.

F. *Delayed Union.* None has been observed so far. On the contrary, Steinmann says that firm union is usually obtained in seven or eight weeks, in some cases even as early as five weeks. The fact that both passive motion and massage can be employed while extension is going on certainly has much to do with prompt callus formation and union. No pseudarthroses have occurred.

III. ADVANTAGES. A. *Traction.* Less weight is needed for any given case than by other methods. More weight can be used than by any other method, and this without the risk of decubitus. The traction is continuous, not spasmodic, as in Codivilla's method or in Lane plating. In cases of long-standing malunion the soft parts may be so contracted that, after freeing their ends, the bones cannot be placed end-to-end without undue tension upon the soft parts which may cause cessation of circulation in the distal part of the extremity or even rupture of important structures. It is in such cases that the continuous traction safely accomplishes its purpose in from three to five days.

B. *Painlessness.* Once the nail is in position there is no pain due to its presence. In fact, after a few days the patients are apt to become careless because of their freedom from pain.

C. *Control of the fragments,* especially of the lower one, is more certain by this method than by any other except the open operation.

D. *The small site of attachment* makes the method available in the compound fractures where other traction methods are either difficult or impossible of application.

Simplicity and possibility of improvisation are qualities of the method which cannot be too strongly praised. Steel drills and the apparatus for driving them, or long nails, together with some

wire or stout cord, are obtainable almost anywhere, and they can be made to serve one's purpose.

The value of the method in military or naval service or in inaccessible regions, is readily apparent. The Prussian army uses it. It is time-saving, effective, and easily learned.

Comparison of Results. With Buck's extension we have more or less shortening and stiffness of the knee, which lasts for a long time afterward. With the Steinmann method there is no shortening, and the transient inability fully to extend the knee-joint quickly disappears. In some cases it is never present.

With Lane plating we have the risk of grave infection if the operation be done by any except the skilled, and in any case, somewhat delayed union. In certain exceptional cases even with no infection, union may be delayed for months, and long immobilization of the knee-joint in such cases has resulted in what amounts to an ankylosis. With the Steinmann method there is much less risk of infection (there have been no fatal cases so far); there is no delayed union (in the average case), and the joints have little, if any, impaired function.

The method of Ransohoff,⁶ whereby the point of a pair of ice-tongs are lightly driven into the bone, is a recent modification of the same principles governing nail extension. The site of attachment with tongs is larger than with the nail.

IV. INDICATIONS FOR USING NAIL EXTENSION. A. *Recent Fractures.* Fractures of the femoral neck constitute debatable ground. Impacted fractures of the neck against the head had better be left alone. Intracapsular fractures in the young show brilliant results when spiked in their proper position at operation. Where operation is contraindicated, Whitmann's abduction is the most rational method for properly approximating the fragments. Pertrochanteric fractures, on the other hand, give excellent results with nail extension (Cases II and V).

In fractures of the shaft, in very obese individuals where adhesive plaster is not effective, nail-extension is indicated (Case VII).

In supracondylar fractures it affords better control of the lower fragment than any other traction method.

In short, nail extension is indicated wherever the usual traction methods fail. A case of von Eiselsberg's, quoted by Steinmann, illustrates this. In a fresh fracture of the lower third of the femur it was found that there was such pressure upon the popliteal artery that the pulse was obliterated. Traction by the usual adhesive plaster did no good. Nail extension was then resorted to and the pulse returned.

B. *Old Fractures.* This is a field which has been practically untouched by traction methods. The fact that nail-extension can

⁶ Lancet-Clinic, August 17, 1912.

be employed with success at a considerable time after the fracture has occurred, makes it of value when a fracture is complicated by extensive abrasions of the skin or by acute disease, such as delirium tremens or pneumonia. Here one can wait until recovery has taken place before applying extension. The method has been successfully used in fractures of forty days' standing in which usual traction methods have been of no avail.

In malunion with much overriding, operation followed by the Steinmann method is the only way in which an ideal result can safely be obtained. The malunion is broken up, and afterward nail-extension is applied. Naturally, larger weights (up to 60 pounds) must be employed. This procedure has been used as late as three to six months' after malunion had taken place.

In pseudarthroses, rubbing of the bone ends together, followed by application of extension, has been suggested. When this is not sufficient the bone ends may be cut down upon and freshened, the wound then closed and nail-extension applied.

As a preliminary to Lane plating in cases where that method is indicated (interposition of soft parts, etc.) nail-extension is excellent, because the absence of shortening lightens the operator's task fully 75 per cent.

To conclude, in certain cases nail-extension is the only method to be used, in others it is an aid to previously existing methods.

I take the opportunity of expressing my gratitude to Drs. Howard Collins, William H. Bishop, A. G. Gerster, John A. Wyeth, Seth Milliken, and Ernest Fahnestock for their kindness in allowing me to employ this method in their services and for the privilege of publishing their cases, the abstracts of which follow (Cases I, II, III, V, VI, VII, IX, and X were presented at the time this paper was read).

SYNOPSIS OF CASES.

CASE I. James L., aged four and one-half years (Dr. Howard Collins' service, City Hospital, Blackwell's Island).

June 26, 1912. A board fell from a building and struck the patient, causing an oblique fracture of the middle third of the left femur. Admitted to City Hospital on June 27.

July 2. Sixth day after fracture. Steinmann two-piece nail; supracondylar insertion. Laughing-gas anesthesia; 6 pounds traction; 1 cm. shortening.

July 9. $\frac{1}{2}$ cm. overcorrection; 4 pounds traction.

July 22. $\frac{3}{4}$ cm. overcorrection.

July 23. Twenty-first day. Nail removed. (X-ray, Fig. 13.)

July 25. Limbs equal; nail holes clean.

August 3. Child can raise entire limb to vertical position; flex and extend knee. Nail holes, two small clean, granulating spots.

October 5. Function perfect; runs and walks without a limp.

Epicrisis. This was a restless, active child who had no pain after the first three days, and who had to be restrained by loops of bandage at the ankle, knee, hip, and armpit in order to maintain proper alignment of fragments (Fig. 14).



FIG. 13.—Case I. Plate taken twenty-one days after fracture; no shortening.

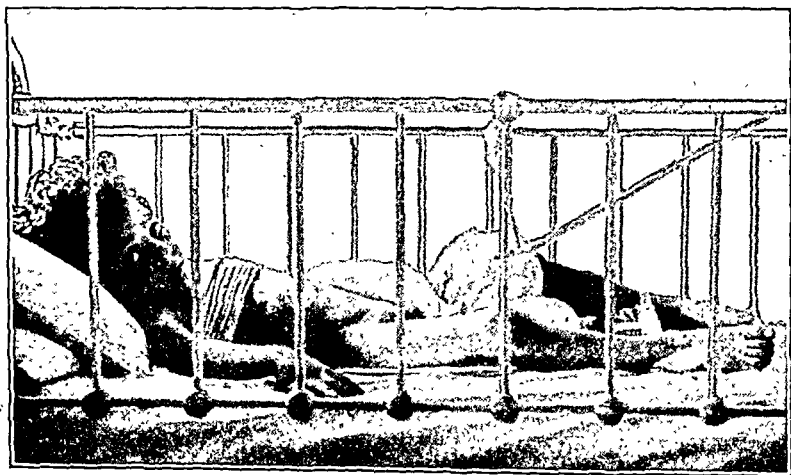


FIG. 14.—Case I. Illustrating restraint necessary with active children to maintain proper alignment of fragment.

CASE II. James R., aged sixty-five years (Dr. Howard Collins' service, City Hospital, Blackwell's Island).

June 14, 1912. Admitted to Bellevue Hospital with a fracture of the neck of the femur.

June 21. Transferred to the City Hospital, with a shortening of $1\frac{1}{2}$ inches and marked eversion.

June 22. Buck's extension with 10 pounds traction applied.

July 1. Sixteenth day after fracture 3 cm. shortening. Steinmann two-piece nail; supracondylar insertion under laughing gas; 21 pounds traction (Fig. 11).

July 12. $\frac{1}{2}$ cm. shortening.

July 18. Eighteenth day after insertion. Nail broke at joint; inner half loose and removed; wet dressing applied to nail hole. Outer half was solid (Fig. 13), and sandbag, which had been placed underneath its end to prevent eversion, and to maintain the limb in proper position, was left undisturbed.

July 19. 1 cm. shortening; x-ray plate (Fig. 15).



FIG. 15.—Case II. Pertrochanteric fracture nineteen days after extension applied.



FIG. 16.—Case II. The same five months later.

July 23. Outer half of nail removed.

July 27. Nail holes healed; good union; massive callus.

July 29. 2 cm. shortening; patient comfortable.

August 14. Patient is encouraged to sit up and to try to walk on crutches.

August 28. Shortening nearly 3 cm.; good flexion and extension; some limitation to inward rotation. Edema of right leg and ankle, which has existed since patient was out of bed on crutches, gradually subsiding under massage.

December 1. Patient has been on crutches for the past three months. Has now been encouraged to walk.

December 23. Bad dermatitis of right leg and ankle from undue use of chloroform liniment.

December 30. *X*-rays (Fig. 16) show neck joined to the shaft at more of a right angle than previous picture; firm union.

Epicrisis. The nail broke on the eighteenth day. Traction was being made by bandages fastened to the projecting ends of the nail. No tongs were available at that time, and it was not feasible to apply other methods of traction. Had extension been maintained for a week longer, it is probable that no shortening would have ensued after removal of traction. Where the two-piece nail has broken with the tongs grasping its ends it has been found possible to still maintain traction, since the tongs hold the fragments of the nail at approximately right angles (see Case XII).

CASE III.—Mary H., aged seven years (Dr. Howard Collins' service, City Hospital, Blackwell's Island).

August 24, 1912. Fell three stories to the ground from a fire-escape, striking a shutter, and other fire-escapes on her way down, sustaining a fracture of the lower third of the right femur. A projecting fragment could be felt in the popliteal space. There was no obstruction to the circulation; 3 cm. shortening.

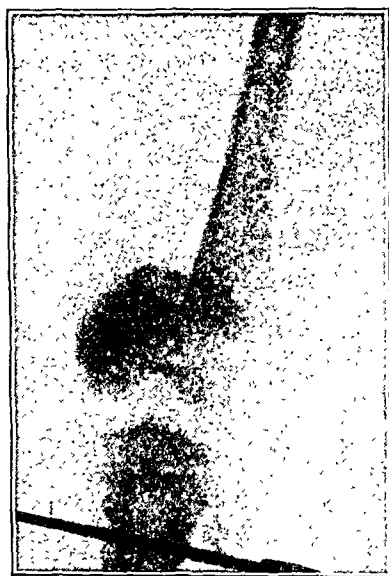


FIG. 17.—Case III. Supracondylar fracture before reduction.

August 26. Second day after fracture. Under laughing-gas anesthesia. A two-piece nail driven through the head of the tibia; 8 pounds traction.

August 28. $\frac{1}{2}$ cm. shortening.

September 3. *X*-rays show lower fragment displaced outward (Fig. 17).

September 9. Reduction of fragment under laughing-gas, by Dr. A. L. Sherman.

September 19. Twenty-fourth day, nail removed.

September 26. Excellent union; patient can raise heel from bed, flex the leg completely, and extend it to within a few degrees of full extension.

October 10. X-rays (Figs. 18 and 19) show excellent position.

October 18. Out of bed for the past few days; can now fully extend leg; limps less and less as time goes on.

October 19. Discharged from hospital.

November 14. Some effusion of knee-joint, which the mother says has been present since leaving the hospital. Limp barely perceptible.



FIG. 18.—Case III. Both knees after reduction.

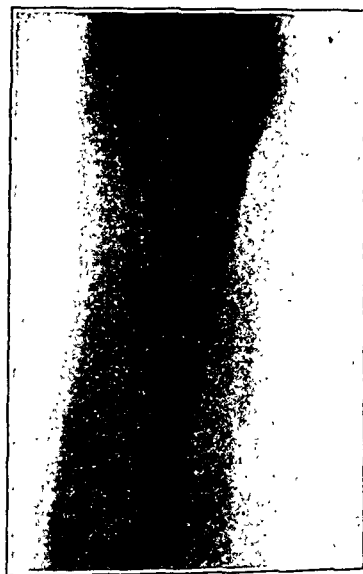


FIG. 19.—Case III. Final result.

December 24. Effusion of knee gone; walks and runs with perfect freedom.

Epicrisis. There was union within one month. Slight limitation to full extension, which was present for a time after removal of the nail, gradually disappeared. The effusion of the knee-joint was present for five or six weeks after discharge from the hospital, and subsided without treatment.

CASE IV.—John H., aged eighteen years (Dr. Howard Collins' service, City Hospital, Blackwell's Island).

September 30, 1912. Was hit by an automobile mud-guard while roller-skating in the street. He was knocked senseless, and sustained a fracture of the middle third of the left thigh.

October 1. A large effusion of the knee-joint. Shortening about 4 cm.

October 3. Fourth day after fracture, Steinmann's two-piece nail inserted through the head of the tibia; 10 pounds traction.

October 5. Shortening 2.5 cm.; 18 pounds traction. Effusion of the knee-joint gone.

October 10. 1 cm. overcorrection.

October 23. Twenty-first day. Nail removed. Some force necessary because of its firm fixation in the tibia.

October 25. Plaster spica applied, reaching to the hip. At this time there was slight lateral mobility, considerable callus, and it seemed as though the upper fragment had moved anteriorly. There was slight lateral mobility of the knee-joint; no limitation to passive motion of the knee-joint.

FIG. 20



FIG. 21

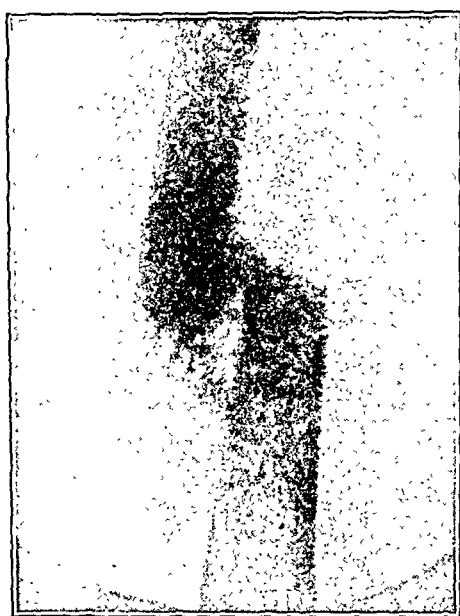


FIG. 20.—Case IV. Transverse fracture seen from in front.

FIG. 21.—Case IV. The same seen from the side. The plate taken at the same time as Fig. 20. was lost, but it showed the same position as this plate (Fig. 21), which, together with Fig. 22 was taken two months later.

October 31. X-rays (anteroposterior view) show good position (Fig. 20). Lateral view (Fig. 21) shows overriding of transverse fragments. This was the first time this case had been x-rayed.

November 6. Cast removed. Up in rolling-chair.

November 15. Patient slipped getting into chair and fell on the floor.

November 17. There was marked bowing and $2\frac{1}{2}$ to 3 cm. shortening. Supracondylar insertion of nail was suggested as the best available traction. This was refused by patient. Because of this, Buck's extension (15 pounds) and lateral traction (15 pounds) at the greatest prominence of the bowing were applied.

November 26. Bowing of thigh has gone; lateral traction discontinued.

December 1. Buck's extension discontinued; 1 cm. shortening present at this time.

December 22. Patient has lain quietly in bed the past three weeks, the leg being in the same position that it was while Buck's extension was being maintained. There was 2 cm. shortening. Flexion beyond 60 degrees limited. Full extension. Some effusion of knee-joint ever since discontinuance of Buck's extension.

December 24. X-rays show good callus and slight overriding of the fragments (Figs. 21 and 22). There is no angulation of the thigh.



FIG. 22.—Case IV. Front view two months later than Fig. 20.

December 30. Home on crutches, with a perfectly solid union.

Epicrisis. There were no facilities for controlling treatment by the x-rays. Because of the extensive effusion of the knee-joint and because of the contusions of the thigh, it was deemed wiser to apply traction to the head of the tibia rather than to run the risk of possibly infecting a hematoma of the thigh. A better result might have been obtained had a solid nail been used in the supracondylar region and had it been possible to follow effects of traction with the x-rays. It seemed unwise to use more than 20 pounds weight with traction on the head of the tibia.

CASE V.—John M., aged thirty years (Dr. William H. Bishops' service, Flower Hospital, New York.)

October 10, 1912. Fractured neck of femur while trying to stop a runaway. His foot slipped and the wheel struck him, knocking him down. An x-ray plate taken at the time showed an extra-capsular fracture passing through and below the greater trochanter.

Unfortunately this plate was lost. There was a shortening of $1\frac{1}{4}$ inches (3.5 cm.).

October 14. Fourth day after fracture, under gas and oxygen; two-piece nail; supracondylar insertion; 15 pounds traction; external rotation prevented by suspending the outer end of the nail to a horizontal bar above the patient which ran the length of the bed (Fig. 7).

November 3. 1 cm. shortening.

November 12. Twenty-nine days after insertion, nail removed; no shortening; can raise knee slightly.

November 14. Plaster spica applied.

December 10. Cast removed (four weeks). Has good function.

December 11. X-rays show excellent position (Fig. 23).

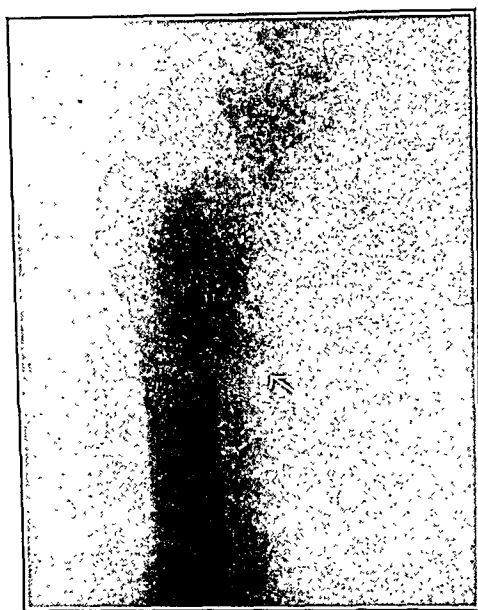


FIG. 23.—Case V. Oblique fracture beginning just below lesser trochanter and going upward through greater trochanter two months after fracture.

December 29. Walks fairly well with one crutch.

Epicrisis. Extension twenty-nine days; cast twenty-four days. Uneventful course. Good result.

CASE VI.—Helen B., aged eleven years (Dr. A. G. Gerster's service, Mt. Sinai Hospital).

October 8, 1912. Was run over by an automobile. Sustained an oblique fracture of the left femur at its middle third.

October 12. Vaginal smear contained gonococci.

October 17. Ninth day after fracture, under gas and ether anesthesia; supracondylar insertion of a two-piece nail; 12 pounds; $2\frac{1}{2}$ inches shortening ($5\frac{1}{2}$ cm.).

October 20. $1\frac{1}{4}$ inches (3 cm.) shortening.

October 24. Equal.

October 27. 1 cm. overcorrection. Traction lessened to 9 pounds. Slight adduction corrected by lateral pull 3 pounds.

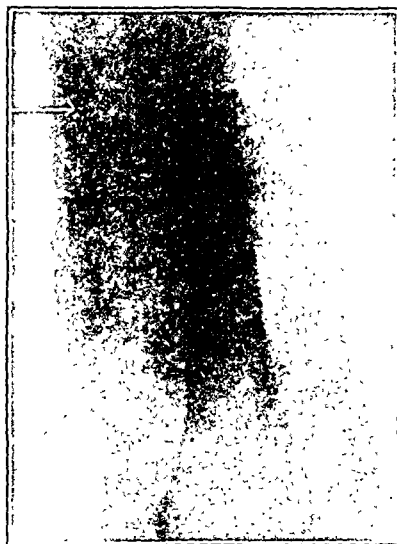


FIG. 24.—Case VI Oblique fracture of the shaft a few days after fracture.

FIG. 25



FIG. 26



FIGS. 25 and 26.—Case VI. After one week of extension.

October 31. Equal.

November 8. Twenty-second day after insertion, nail removed. Good fibrous union. Slight false point of motion.

November 9. Pain in the right loin. Temperature, 100° .

November 10. Vomited a number of times; pain in right loin increased; temperature, 104.2° ; urine contained many red blood and pus cells.

November 11 and 12. Temperature, 103° to 104° . Gradually subsided by lysis. Nail holes healed.

November 14. Cast (spica) applied to hip and thigh only, allowing movement of knee.

November 15. Temperature normal.

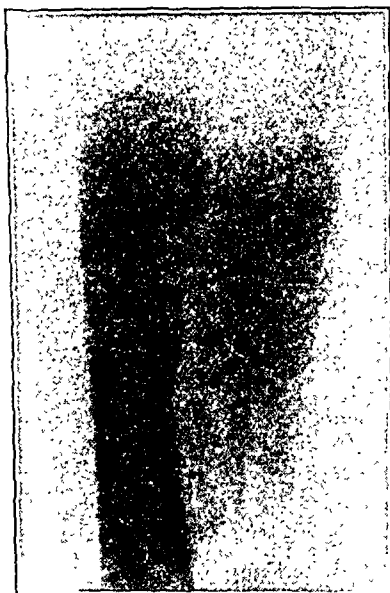
November 21. Urine contains very little pus; no albumin.

November 23. Cast removed; no shortening. Some bowing of the leg anteriorly. Has been walking on crutches for the past five days.

FIG. 27



FIG. 28



FIGS. 27 and 28.—Case VI. Final result eleven weeks after fracture.

November 25. Discharged.

December 23. Fell and bumped knee.

December 27. Returned to the hospital for x -rays, which show good position (Figs. 27 and 28), Moderate effusion of the knee, which was treated with cold compresses.

Epicrisis. Nail applied on the ninth day remained in place twenty-two days. Convalescence complicated by a smart pyelitis, probably due to the vaginal infection. Slight anterior bowing, probably due to lack of support below knee while patient was wearing plaster cast. No infection of nail holes. This was the only case of the entire series in which it was possible to follow the effect of traction with the x -rays.

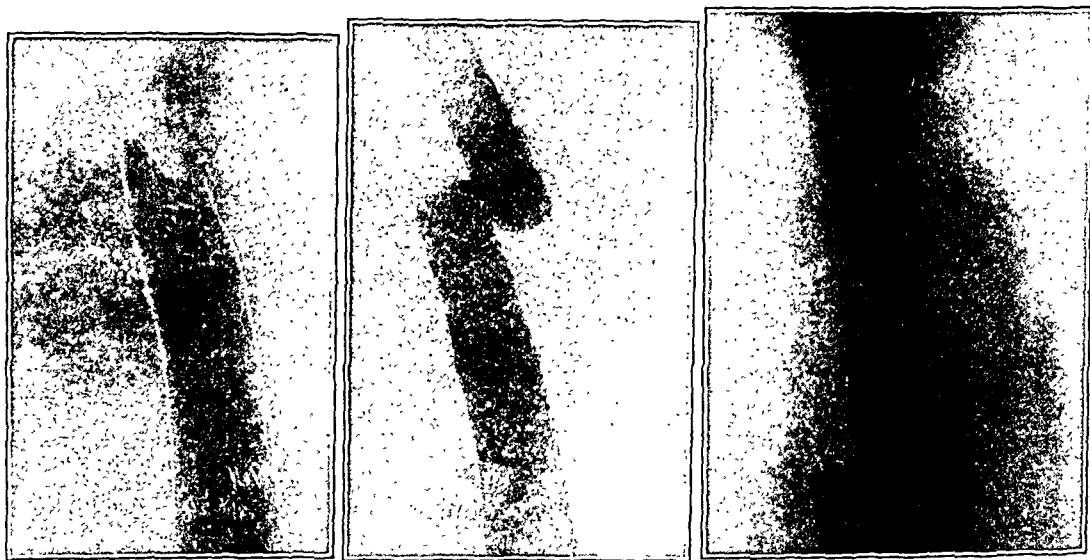
CASE VII.—Michael N., aged fifty-four years (Dr. S. M. Milliken's service, Lincoln Hospital, New York).

An extremely stout man who had varicosities of both legs for a number of years past. Non-alcoholic. He had been so asthmatic that he had been unable to work for the past six years. Five months before fracturing his thigh he contracted erysipelas of the right leg, and had stayed at home until the day of fracture, September 22, 1912, when he went out. He tripped stepping off a curb on his way to church and sustained a fracture of the upper third of the right thigh. Was taken to the Lincoln Hospital, where it was found, that besides the fracture, he had a mitral insufficiency and was extremely emphysematous. There was one inch shortening and marked eversion. A plaster spica was applied. The cast compelled him to lie flat; he nearly suffocated from his asthma that night, so that the cast had to be cut away from the abdomen in order to permit his sitting up.

FIG. 29

FIG. 30

FIG. 31



FIGS. 29 and 30.—Case VII. Tracing of fracture of shaft in an obese man, 250 pounds, about 5 feet 4 inches high, two days after fracture.

FIG. 31.—Twenty-five days later; good callus.

September 23. (X-rays, Figs. 29 and 30).

September 24. Cast removed.

September 26. Fourth day after fracture, shortening approximately $1\frac{1}{2}$ inches. Steinmann solid nail 21 cm. long; supra-condylar insertion. The thigh was so thick that the nail ends barely projected. No anesthesia; pain not extreme.

September 27. Tongs applied; 15 pounds traction.

October 2. Traction increased to 30 pounds; one inch shortening.

October 16. Nineteenth day, nail removed. Local decubitus from tongs where they grasped the end of the nail. Three-fourths inch shortening; no anterior motion; slight lateral motion.

October 17. X-rays (Fig. 31) show slight overlapping and large callus.

October 25. Dressing removed; wounds healed.

November 1. Lifted entire leg from bed; active motion.

November 12. Stood up for a moment (the first time) while being weighed; weight, 250 pounds. Out of bed in chair.

December 1. Out on crutches; no limitation of motion.

December 8. Discharged; on crutches.

Epicrisis. An obese asthmatic individual, wholly unsuited for Lane plating or the usual Buck's extension, in whom the nail-extension gave most satisfactory results.



FIG. 32.—Case VIII. Taken shortly after fracture.

CASE VIII.—Arthur A., aged twenty-seven years (Dr. Ernest Fahnestock's service, J. Hood Wright Hospital, New York).

November 8, 1912. A counter-weight of an elevator struck his left thigh, causing a fracture at the middle third and rupture of the internal lateral ligament. (X-ray, Fig. 32.)

November 22. Fourteenth day after fracture. Had been in a posterior splint for the past sixteen days. Slight fever ever since admission; 9 cm. shortening. Two-piece nail; supracondylar insertion; laughing-gas anesthesia; 16 pounds traction.

November 23. Temperature, 102°. No local discomfort. General condition good.

November 24. Temperature normal. Traction, 21 pounds.

November 25. 2 cm. shortening. Traction increased to $23\frac{1}{2}$ pounds.

December 1. 1 cm. shortening.

December 4. No shortening. Edema of leg, which was present up to now, is nearly gone.

December 24. Upon releasing weights there is 1 cm. shortening; plenty of callus; still some motion.

December 26. Nail removed (thirty-fourth day); 1 cm. shortening afterward.

December 29. $2\frac{1}{2}$ cm. shortening; nail holes clean; union improving; 30 degrees motion in flexion of knee (X-ray, Fig. 33).

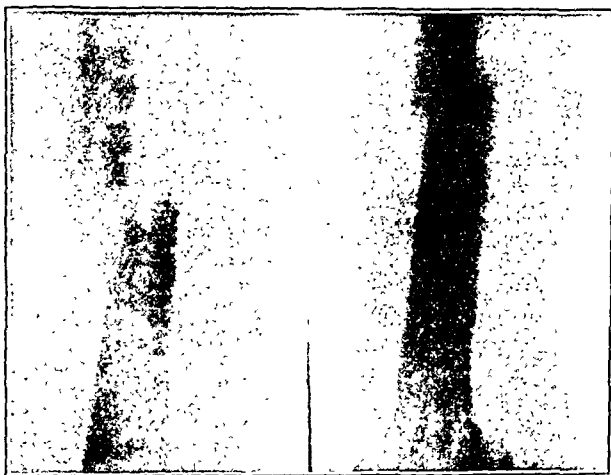


FIG. 33.—Case VIII. Two months later. The nail extension was applied fourteen days after fracture (9 cm. shortening). At present 1 cm. short—front and side view.

January 3, 1913. Firm union. Function of knee much better.

Epicrisis. Nail-extension was applied fourteen days after fracture and was maintained thirty-four days. The 9 cm. shortening on the sixteenth day was reduced to *nil*. There was delayed union. This accounted for the shortening which came after discontinuance of traction. A two-piece nail was used, and it was deemed unwise to use more than 23 pounds traction for fear of breakage.

CASE IX.—Charles H., aged fifty years (Dr. John A. Wyeth's service, Polyclinic Hospital).

November 22, 1912. Patient was standing on the end of a freight train, which was backing down. The train suddenly stopped, threw him off, and he became unconscious. He sustained a traumatic amputation of the big and second toes of his right foot, a fracture of the upper third of his right femur, and a concussion of the brain.

November 25. Third day after fracture, solid nail inserted under laughing-gas anesthesia; 12 pounds traction; one inch shortening.

November 28. No shortening. Traction wire broke.

December 1. 1 cm. shortening.

December 16. Twenty-first day, no shortening; apparent union; nail removed; removal required considerable force.

December 21. Wounds healed promptly.

December 30. X-ray (Fig. 34). Revealed a badly comminuted fracture of the neck and trochanter. The fragment indicated by the arrow was palpable and led to the diagnosis made above. Today there is three-fourths of an inch shortening. Abduction will be maintained by a cast.

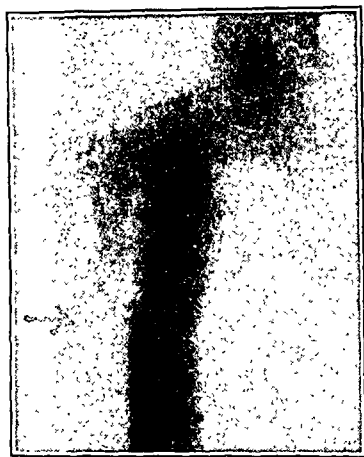


FIG. 34.—Case IX. Comminuted fracture of greater trochanter and shaft (thirty-eighth day).

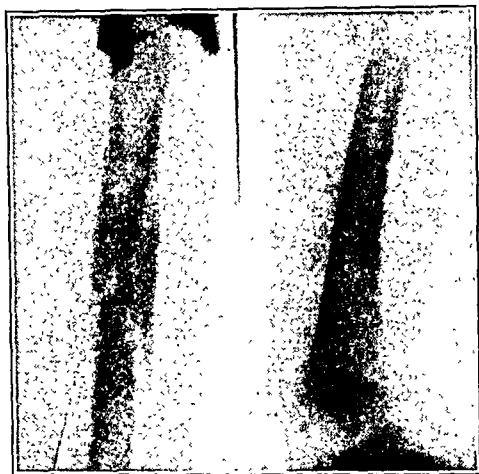


FIG. 35.—Case X. End-result six weeks after comminuted fracture of shaft. No shortening.

Epicrisis. The crushed condition of this man's foot would have made proper attention to it difficult had a Buck's extension been applied. As it was, dressings were not hindered by the nail-extension apparatus. This case emphasizes the value of controlling clinical observations by the x-rays.

CASE X.—Charles C., aged nine years (Dr. Ernest Fahnestock's service, J. Hood Wright Hospital, New York.)

November 23, 1912. Patient was hit by an automobile and sustained a fracture at the middle third of his left thigh.

December 2. Eight days after fracture there is a large effusion of the knee-joint. 2 cm. shortening. Under laughing-gas anesthesia; a solid nail inserted through the head of the tibia; 10 pounds traction, which was increased later to 15 pounds.

December 4. 1 cm. overcorrection; effusion less.

December 13. Effusion of the knee-joint gone.

December 24. Twenty-one days after insertion, nail removed easily; good union; large callus.

December 29. Nail holes clean. Can raise knee twelve inches from bed; active or passive flexion beyond this is painful.

December 30. Out of bed on crutches. (*X-ray*, Fig. 35.)

CASES IN WHICH NAIL-EXTENSION WAS APPLIED AND WHICH
DIED FROM CAUSES HAVING NO RELATION TO THE
METHOD EMPLOYED.

CASE XI.—Alice K., aged fifty-two years (Dr. Collins' service, City Hospital).

September 13, 1912. Patient broke her right hip.

September 20. Supracondylar insertion of Steinmann's two-piece nail by Dr. H. H. Janeway.



FIG. 36.—Case XI. Total absorption of femoral neck three days after fracture in a syphilitic subject. The head lies against the shaft.

September 21. Wassermann reaction was reported strongly positive. On account of her debilitated condition, she bore antisyphilitic treatment poorly.

October 7. Seventeenth day after insertion, local pain around the nail; temperature, 102°.

October 10. Twentieth day, fever having continued, nail removed; 2 drams of pus escaped; nail was found broken at the screw-joint; but the ends of the tongs had kept the pieces of nail in position at approximately right angles to the bone.

October 11. Temperature normal; discharge less.

October 15. No union. X-rays show total absorption of the femoral neck, so that head rests against shaft (Fig. 36).

October 18. The patient has been gradually declining for the past two weeks. During the past week there has been no fever; she became much weaker this day; went into coma and died. Diagnosis: Death from syphilitic myocarditis. No autopsy.

Epicrisis. This was a fracture of the neck of the femur in a markedly syphilitic subject. Total absorption of the neck in thirty-two days. It is possible there was a previously existing gumma of the neck of the femur, predisposing to fracture at that point. The patient was intractably filthy in her habits. Inflammation of the nail hole, which occurred on the seventeenth day after insertion, promptly subsided after removal of nail and application of wet dressing. Patient died of her myocarditis a week after her temperature had reached normal. The nail broke at its joint under no undue strain. (Traction between 10 and 15 pounds.)

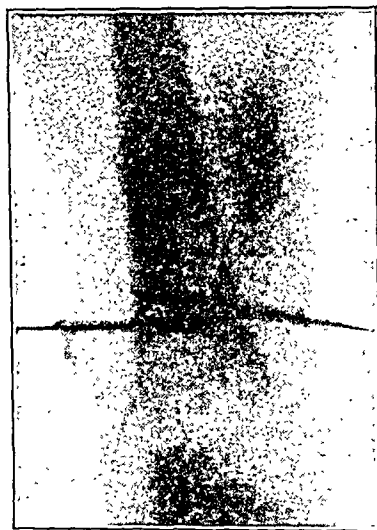


FIG. 37.—Case XII. A two-piece nail which broke at the joint. The pieces were held at approximately right angles by the tongs and continued to exert traction.

CASE XII.—Fritz D., aged forty-eight years (Dr. Collins' service, City Hospital).

October 27, 1912. A confirmed drunkard, fractured his thigh while intoxicated. Had delirium tremens four days after admission. Moderate icterus. Condition gradually improved.

November 1. Two-piece nail inserted; no anesthesia; 19 pounds traction.

November 2. Comfortable.

November 3. Again developed delirium; irrational. Developed a pneumonia, to which he promptly succumbed.

November 5. X-rays, taken while in delirium, show broken nail held in place by tongs (Fig. 37). No autopsy.

THE RELATIONS OF INTERNAL SECRETION TO MENTAL CONDITIONS.¹

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THE subject of internal secretion has aroused much interest among physicians during the last decade, and detailed investigation has furthered the work. As a matter of fact the relations of glandular secretions to the nervous system have been noteworthy. We find observations on the influence of the secretions on psychic conditions, to which may be added attempts to influence certain psychic conditions curatively by organic extracts (opotherapy), also the scientific movement which defines changes in the glands as phenomena resulting from psychic anomalies.

Nor have attempts been lacking to present clearly the matters in question, particularly the report of Laignel Lavastine at the Congress of Dijon and the reviews of Bauer, Marburg, Muenzer, and others.

Observations on operated animals are of particular importance, the investigations on the hypophysis by Cushing, Aschner, and others being interesting examples.

In the effort to give an outline of our present knowledge, based on the work done by myself and other investigators, I feel that the facts are incomplete, that hypotheses must play too great a part therein. Still, the investigations have accomplished sufficient to present a review which is not uninteresting, and it is necessary to compile such a review, premature though it may seem, if only to point out the way which future studies must follow.

The oldest problem of internal secretion is the action of the genital glands. The peculiar effect of the testicle extracts observed by Brown-Séquard was the first evidence of an internal secretion.

In older literature it was affirmed that not only the entire nature of woman, but her character as well depended on the reproductive organs. Heimont said, "Propter solum uterum mulier est quod est;" Chereau said, "Propter ovarium solum mulier est, quod est;" and Virchow's statement that a woman is a woman simply because of her generative gland is familiar. The peculiarities of her body and mind—in short, all the femininity which we admire in the true woman—are dependent on the ovary. This interpretation is not unimportant if we reflect that modern study of the brain, otherwise so rich in results, has not succeeded in discovering differences between the male and female individual

¹ Lecture delivered at the Medical Department of University of California, September 3, 1912.

which would be able to explain the psychic differences between both sexes.

So long as the genital glands do not enter into energetic function—in childhood—the secondary sexual characters are scarcely indicated. The psychic differences are often recognizable as early as the second and third year, become more marked in later years, and the differentiation becomes pronounced only after puberty. The study of this period of development becomes the more interesting when we compare the powerful *ascendente* with the later *decescente* of the climacterium in man and woman.

Let us begin with man. Puberty is preceded by a certain unrest, a noticeable vacillation, sometimes a sort of fear; only then the erections and pollutions begin. The voice changes—it becomes rougher and deeper. The thyroid gland becomes larger; the genital and axillary hair appears, and the body grows more hairy in general; the beard becomes apparent; the epiphyseal cartilages begin to ossify. The psychic changes come into the foreground; childish plays are dropped; reading takes a higher course. New energy takes possession of the young man—the ambition to perform great deeds, to act for great ideas, and frequently the inclination to solve the world's problems. Anxious doubts as to the doctrines of religion, hitherto believed in with childish simplicity, vary with emanations of an unhealthy and exaggerated religious faith. Diffidence alternates with self-confidence and self-consciousness. Plans of reforming the world are formed. Conduct toward the female sex is strained. Games with girls are regarded with scorn, and the opinions of women in general are held in contempt. In odd contradiction to this, bombastic declarations often come freely from their lips; they are bashful in their association with women; and they adore some particular female, whom they would never venture to address, with the romance of a troubadour. Here we see strongly indicated what every man retains in some measure, and what every woman possesses—a certain unconscious antipathy, in some respects, to the other sex. There is here something mysterious—something that cannot be bridged over. In these young men there is also often a tendency to mysticism. Eroticism and mysticism are matters which often go hand in hand. It is the age of sentimentality, in which the German youth tries with more or less success to sing in the rhythm of Heine.

However, especially in those with a neuropathic tendency, this sentimentality becomes too deep. This is the times of the steadily increasing number of youthful suicides; also the appearance of youthful psychoses, which in their incipency so often present a caricature of awakening sexual life.

The period of sexual tempest in adolescence is succeeded by the period of young manhood, also dominated by strong sexual emotions, which now follow quieter paths. But the tempestuous

still has the upper hand. The age of genuine love begins, which cannot be explained scientifically. The cortical excitability increases; often, also, the intellectual capacity. Birds sing at the time of mating. Man's imagination broadens; the poets sing their best songs; the musicians compose their most beautiful music; discoverers and inventors often do their best work when in love (Ostwald).

In observing the processes before and after coitus the influence of the secretion of the sexual gland is much in evidence. The strong, stormy, psychic excitement, at times combined with a certain mental incapacity, which precedes coitus is often followed by a sort of transitory antipathy to the same woman so passionately longed for a short time before. Coitus at normal intervals acts favorably on the mental condition, and excesses are injurious.

Observation of onanists gives further proof of the influence of genital secretion. It is generally believed by physicians that isolated onanic acts do not materially injure the individual, but when the secretion is excited too often those who are addicted to this habit become weak, abulic, averse to society, and show decrease of intelligence and memory.

The much-discussed question of sexual abstinence in vigorous men must be here touched upon. Some men seem to tolerate easily this abstinence, but in others psychic symptoms may be observed in the stage of abstinence, unrest, melancholy, general discontent, symptoms which sometimes decrease after sexual satisfaction. This symptom-complex seems to occur more often in persons with a neuropathic tendency.

Men also present a peculiar picture at the time of cessation of the internal secretion of the genital glands, although not in the same degree as woman at the critical age. The picture has been described in detail by Mendel. We have to deal mostly with men of forty-seven and fifty-seven years of age, who show reduced or absent sexual desire and potency, but who were often previously healthy and strong. Now they are nervous, emotional, often break into tears, have attacks of perspiration, palpitation of the heart, show lassitude, and are sleepless. At times they have attacks of giddiness and headache; often there are diffuse bodily pains and paresthesias. The memory grows dull, mental interests decrease, and the patients manifest hypochondriac ideas.

But other psychic changes in aging men, changes that are beneficial to humanity, must not be forgotten. At the decline of sexuality psychic rest often develops—peaceful calm, a clear view and review of life, and a tendency to mildness. These are the men who no longer produce new and enthusiastic ideas, but who as teachers and guides fully grace their position. As judges they are in their fittest place. The men with strongly secreting genital glands have too much temperament for such office, and

too much passion. A German statesman is alleged to have said that only two things grow better with age, wine and judges.

Experiences in regard to castration are particularly instructive. In the animal kingdom this operation is often practised on domestic animals—stallions, bulls, rams, cocks, and birds. We know that if these animals are castrated early they not only develop differently in body, but change their psychic conduct and lose their liveliness and aggressiveness. Not only is the outward appearance of the early castrated known, but the peculiarities of their character have been often discussed; they are thought to be cunning, secretive, avaricious; they often love dress and jewelry to excess, and they have no great executive ability. Moebius states that in Italy eunuchs have frequently had great success as music virtuosi, especially as singers; but that in productive art, that is, composition, they are not successful. The influence of late castration, mostly for surgical reasons or because of injuries, has been frequently discussed in literature. In these persons bodily changes are little noticeable; on the other hand, conditions of depression and psychoses are found relatively often.

In certain conditions associated with inferior or undeveloped genitals, in infantilism and eunuchoids (Tandler and Gross), lighter or more severe degrees of imbecility are not infrequently found. Men with even slight genital affections often suffer from severe depression.

From what has been said, we see what a great influence the genital organs, with their secretion, have upon men.

In regard to women, we find that the time of puberty is characterized not only by the somatic signs of the appearance of menstruation and the secondary sexual attributes, but also by psychic changes. Young girls become restless, nervous, apprehensive, dreamy. Months often pass before the proper equilibrium is reestablished. The psychoses present at this time differ from those in boys. The progress of intelligence becomes marked in boys during the puberty. Girls between the ages of eighteen and twenty-two, that is, when sexual conditions have calmed down, often attain a remarkable mental elevation (Moebius). The strong imagination, quick conception and comprehension are often remarkable at this age.

In the further progress of her life the periodical menstruation shows not only somatically as bleeding, but also in the entire make-up of the woman and here, again, psychic factors are evident. Menstruation is preceded by a certain irritability and a slight psychic stagnation. When the hemorrhage appears women have a feeling of lassitude, become abulic, and less active intellectually. Icard (in Havelock Ellis, from whose studies we quote liberally) observes that in perusing the diary of a young girl it does not require much perspicacity to discover the pages which were written

during menstruation. Among 80 women who were arrested for resisting the police, Lombroso found only 9 who were not menstruating. Among 56 female shoplifters, Legrand du Saulle found 35 who were unwell at the time of the crime. Suicides are known to be frequent at the time of menstruation. A. Pilcz found intra-menstrual changes of the sexual organs in more than one-third of female suicides. The question of the not infrequent insanity during menstruation has likewise been discussed. Recent investigations have shown that menstruation in women is not a suddenly appearing and disappearing event. On the contrary the organism seems to be in a continuous wave-like movement which is not found before the beginning or after the close of menstruation in childhood or old age. Perhaps the much-discussed variability of mood may be explained thereby, the often inexplicable vacillation of mood in the sexually mature woman.

Pregnancy and the puerperium play a peculiar part in a woman's life. As regards the puerperium, we have to deal only with that which takes its course without fever. Even women otherwise not psychopathically inclined usually become nervous and easily depressed during the time of pregnancy. Neuropathic natures at such times often have a tendency to severe depressions, with a tendency to suicide. The frequency of psychoses in this condition is well known. In exceptional cases, remarkable contrasts to this picture are observed. Some women almost habitually suffer from severe depression, being mentally most calm, even during pregnancy.

The psychic disturbances of the climacterium, the most dangerous and critical age of woman, have also been much discussed. At the time when menstruation begins to be irregular—sometimes even months or a year before—women fall into a strange state of unrest, sometimes accompanied by sexual overexcitability. Deep depressions, a tendency to outbreaks of weeping, periods of irritability, psychic vacillation, and a decrease of intelligence are well-known conditions in most women at this time. But in some cases it reaches a high degree: psychoses of depressive character are often established. The gossipy character of the old hag has also been much discussed. The messenger of misfortune in fairy tales is almost always an old witch. If for reasons of local diseases castration is performed in women, phenomena appear, similar to those above described, only less pronounced and the effect of late castration on the mental condition is not nearly so great as on men; but literature has many examples of psychoses after the operation mentioned. Nothing accurate is known about the psychic condition of women after early castration. The undoubted influence of genital affections of the most varied kinds on the mental condition of women has been much discussed. How deeply rooted the conviction of this influence has been is shown by the opinion of the connection between hysteria and the genital organs and by

the repeated attempts of gynecologists to cure serious hysterias by castration.

The thyroid gland is the most interesting organ for the study of internal secretion. It is indeed the only organ in which we can differentiate hyperfunction and hypofunction clinically, and experimentally. The hyperfunction appears most distinctly in Basedow's disease. In 1909 R. Stern in Noorden's dispensary, reviewed my Basedow material, covering a period of twenty-five years, and found that we must distinguish certain definite groups. Basedow's disease is marked by rapid beginning and rapid growth of the struma, by pronounced trembling, extraordinary tachycardia, and increasing exophthalmos. These typical affections mostly befall individuals without hereditary tendency. In a number of cases, however, we have to deal with hereditary affected individuals, mostly persons who have for years been suffering from nervous symptoms (degenerative Basedow).

But the recognition resulting from investigation, that the so-called "formes frustes" differ greatly from the principal ones and have the tendency to change into the genuine, is important. They must be considered as a separate group of diseases. There are individuals who even in youth have a struma, though only a moderate one, which usually does not grow, or very little, afterward. The other symptom-complex develops sporadically only, and not to an unusual degree; the exophthalmos is often altogether absent or only indicated. In this group the mental condition is also changed. They are often grumbling, hypochondriac, melancholic, and egotistic persons.

The study of the cases is more important in which psychic anomalies may appear in various forms. But one tendency is often pronounced—namely, the predominance of manic features. The individuals are often excited, though we cannot exactly speak of a psychosis. They are talkative, spasmodic in their thoughts and actions, and sometimes incline to witticisms. In conversation they often prefer erotic subjects, and are given to sexual excesses. In the acute psychoses of these patients there may be a predominance of manic features.

I remember the first case in my practice. It was that of a woman, aged twenty-one years, who grew rapidly nervous, and in whom there developed simultaneously the various components of the typical Basedow, with an unusually excessive exophthalmos. Except for a certain excitability the patient seemed normal, and she was sent to the seashore. But her mental condition changed for the worse. I hastened to see her, and when I entered the gate she came to meet me, singing gaily, her hair loose and wreathed with flowers. The physical disease lasted for several weeks. The excitement, which had abundant erotic features, grew considerably. There was no defect of intelligence, no pronounced confusion of

ideas, no hallucinations. After a few months the condition improved. Gradually the permanent cure of the psychosis resulted and at the same time the Basedow symptoms disappeared.

Opposed to the picture of Basedow disease, of hypertrophy of the thyroid gland tissue, we have the picture of atrophy and degeneration. The somatic and psychic pictures bear the relation, says Weigandt, of the photographic positive to the negative. Most striking is the condition of the adult myxedematous patients, with the typical absence of the thyroid gland. The principal factor is the complete lack of emotion. A considerable role is ascribed to the thyroid gland in emotional life. According to Levi and Rothschild it is the "glande de l'émotion." The similarity of the picture of fear emotion and that of Basedow's disease should be remembered, also the lid fissures, the protuberance of the bulbi, the trembling, the tachycardia, the congestions which alternate with pallor, the outbreaks of perspiration, the diarrheas, the trembling of the legs.

As emotional as are those afflicted with Basedow's disease, so lacking in emotion are the myxedematous. According to Charcot they may be compared to hibernating animals: dull-witted, indifferent, unable to work, disinclined to sexual activity, the memory gradually decreases, the power of judgment becomes minimal, and the patients often lie in bed apathetically for days, almost without desire for food or drink. Severe psychoses are by no means rare in these patients. The connection between the mental condition and lack of the thyroid gland may best be studied if thyroïdin be administered for therapeutic purposes. It is then often surprising to see the apathetic and indifferent become lively and communicative and evince signs of intelligence which would not have been considered possible a short time before.

The significance of the thyroid gland also becomes clear on examination of children with congenital or acquired myxedema. The mental inferiority of cretins, with defective or degenerative thyroid glands is well-known. The psychic picture may be improved by administering thyroïdin (Wagner-Jauregg).

Muenzer refers to the well-known swelling of the thyroid gland, with processes in the genitals, in puberty and in pregnancy. In gravidity the hypophysis shows marked changes. There is a mutual action between the glands—every affection may be polyglandular—and some attribute the affection to a single gland.

We cannot leave this phase of the subject without a word on the parathyroid glands, the four accessory glands of the thyroid, which differ from the genuine not only in histological structure, but also in function. Clinical investigations (Jaendelize, Pineles, Vassale, Jenerali, Erdheim, and Riedl) have shown the probability of tetany being a consequence of the affection of these organs. In 1889 I described psychoses in individuals who had fallen ill of typical tetany.

At the culmination of the affection, which in Vienna appears in March and April, typical tetanic attacks appeared which subsided with the symptoms of somatic affection. Similar cases were also described by other authors, especially cases of a strumipriva or parathyreopriva form. The mood of those afflicted by tetany is not to be designated as normal, even if we do not consider the actual psychoses. These individuals are excitable, timid, uneasy, quarrelsome, and inclined to outbreaks of temper. Depression is occasionally present, but is not one of the dominant symptoms. In the psychoses the conditions of temper and excitement predominate. I found among my old patients with tetany several who had grown excitable and irritable. In those who had myxedematous phenomena the symptoms of mental lassitude appeared which were not recognizable in the other forms.

In strumectomized animals peculiar psychic changes have been described. Blum mentions hallucinations in strumectomized dogs, as well as changes of characteristics, idiocy, and pathologic motion phenomena. Horsley and Pineles saw similar phenomena in monkeys. Erdheim observed conditions of excitement in rats, and stated that these are connected in some way with tetany, as on the days when the animals are excited tetany often reappears.

Our knowledge of the thymus gland is still small, though Basch and Klosevoigt referring to the feeble intelligence of animals whose thymus had been extirpated, speak of an "idiotic thymopriva."

We know more about the so-called brain glands, the hypophysis (pituitary body) and the epiphysis (pineal gland—glandula pinealis), and during the last decade many important side-lights have been thrown on the question of their influence on mental condition.

Engel of Vienna, in his dissertation on the pituitary body in 1839, gave expression to his ideas on this subject.

The hypophyseal affections have to be divided into two large groups, the acromegalia and the dystrophia adiposogenitalis (Fröhlich's type). Psychoses of various kinds in these conditions have been described. Schuster has treated this subject in detail. He found that tumors of the corpus callosum probably cause psychic disturbances; frontal lobe tumors, 80 per cent., temporal lobe tumors, 66.6 per cent., the hypophyseal tumors, 65.3 per cent.

Boyle and Beadles among 3000 necropsies at the lunatic asylum found tumors in 20, 6 of them hypophyseal. The number of actual hypophyseal psychoses is somewhat overestimated. Large brain tumors which because of increase of brain pressure and destruction of brain parts may *eo ipso* call forth psychoses are encountered. But the fact that psychoses are so frequent in affections of the pituitary body gives food for thought, in spite of their association at times with destruction of tissue in other parts of the brain. I have seen many pituitary body tumors, and have noticed a

psychic change, a peculiar indifference, a certain contentment, a euphoria which is not in harmony with the symptoms, such as headache and blindness. The patients are calm, and have a childish confidence in the doctor. The sleepiness of the patients is pronounced, but if they are forced to arouse themselves, their intelligence has not suffered nearly so much as we would be led to believe by the outward impression they make.

The psychic factor may best be studied by observing operated cases. I have seen cases operated on either by the Schloffer (cases of v. Eiselsberg and Hochenegg) or the nasal method of Hirsch. It is remarkable how lively, agile, and communicative the patients become. The entire psychic condition of the corpulent partakes of the condition of individuals with constitutional obesity. The peculiar mental slowness, indecision, good nature, and sleepiness of these people is proverbial. Loss of hair is not uncommon.

It is not uninteresting to compare the acromegalic with the physiologic giants. They often have a peculiar heavy manner and lack of initiative. The psychic peculiarity of hypophysis patients, which we described in our report at the International Congress at Budapest in 1909, is of interest from the fact that the animal experiments of Cushing in Baltimore and Aschner in Vienna showed that in hypophysectomized dogs the psychic changes corresponded with those of human beings. According to Cushing, animals with hypopituitarism become psychically abnormal: at times they are lazy and sleepy, then playful and excited.

If in early childhood tumors (teratoma) develop on the glandular pinealis a picture is presented which is more intelligible since the observations of Gutzeit, Ogle, Oesterreich, Slavik, Neumann, Marburg, Bailey, and Jelliffe. The features of premature sexual development are combined with an unusual development of fat. In a boy, aged four and a half years, who had always been very large and somewhat fat, the genitals developed remarkably. In his fifth year erections appeared, the voice became deep and hoarse, and the body showed a hirsute appearance which corresponded to the age of eighteen or twenty years. He had the symptoms of a cerebral tumor (headache, vomiting, epileptic attacks, paralysis of the eye muscles, and choked disk). He died of scarlatina. The necropsy findings showed a teratoma of the pineal gland. One point in this observation is of importance, the early development of the mental condition. The boy was overintelligent, and had an inclination to discuss ethical philosophic questions. In his fifth year he showed the same psychic peculiarities that are displayed by youths during the development of puberty.

There were also signs of early psychic development in the cases of Oesterreich and Slawyk and Raymone and Claude. The hypothesis therefore was that the pineal gland was to be considered among the blood glands, and that it influenced genital development. Its

absence causes premature genital development and psychic development corresponding to the age of puberty. Descartes placed the seat of the soul in the pineal gland, and although in this form his belief cannot be upheld, still when a genius has once made an assertion, something of it will always remain.

Of the abdominal glands the pancreas and its internal secretion play a large part in relation to diabetes. Diabetics often show mood anomalies, and we speak of actual diabetic psychoses. We have no test for determining how far the psychic peculiarities depend on the secretory disturbances of the pancreas.

The study of suprarenal capsule affections gives us more positive points of knowledge. The secretion of these organs and their effect on the nervous system are generally known. The connection between disturbances of brain development and hypoplasias of the suprarenal capsules, is of importance in the subject under discussion. Leri in 3 cases of melancholia found destruction of the suprarenal capsules. At the clinic there are occasional cases of Addison's disease with a tuberculous destruction of the organs mentioned. These individuals are weak, exhausted, and hopeless, in contrast to the euphoric patients with tuberculosis of the lungs. Irritability and depression are almost always present.

Psychoses of various kinds have also been observed in which depression seems to predominate. In addition to the observations of Leri, we refer to the histories of Bonhoeffer, Vollerecht, Rodionow, Boinet, and Klippel.

From this review it will be seen that we know of a number of the effects of internal secretions on mental conditions, and how the development of the mind depends on these secretions. Brain anatomy helps but slightly in showing how higher mental development is to be explained. Perhaps the time will come when we shall learn to perceive how much depends on the individual structure of certain glands and on their individual internal secretion.

AN EXPERIMENTAL STUDY OF SODIUM BICARBONATE AND OTHER ALLIED SALTS IN SHOCK.

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IN recent literature there is a vast preponderance of work on the various possible causative agencies of shock and practically a

dearth of investigations directed toward the therapeutic relief of this serious symptom-complex. Howell¹ in 1903, was led by a laboratory accident to investigate the physiologic action of sodium carbonate and found this salt to be an excellent cardiac stimulant in shock. Henderson,² in 1910, as a result of his extensive investigation of acapnia, suggested as a rational therapy for shock the prevention of loss of carbon dioxide (the carbon dioxide being lost chiefly as a result of hyperpnea and by exhalation from exposed viscera) and the replacement of such loss, as had previously occurred, by increasing the dead space of the respiratory tract. These two investigators furnish about the only new lines of therapeutic thought developed during the past decade on the subject of shock.

Howell's work is important in that it demonstrated both the pronounced action of sodium carbonate on the force of the heart beat and also the duration of this effect over a comparatively long period of time. According to Howell, the rate of beat was unaffected, and vascular tone, likewise, in all probability was not influenced. In severe degrees of shock, sodium carbonate did not yield the brilliant results secured by the use of this same drug in the more moderate cases (where the blood pressure registered 60 to 70 mm. of mercury); but even so, to quote Howell, the results were more hopeful "than those obtained by the use of other substances suggested as having value. Adrenalin, hypophysis extract, alcohol, and strychnine gave negative results or, at best, temporary and unimportant rises." The nucleus of Howell's work, though not expressly so stated by the author, lies in the thought that the pressor effect of sodium carbonate is due to its alkalinity. Dawson³ extended Howell's work by using sodium bicarbonate, but in his experiments he induced shock by bleeding his animals, thus complicating an already complex set of phenomena by the added element of hemorrhage. Henderson's work, in its turn, is important in that it reviews and reemphasizes the importance of carbon dioxide as a body hormone, and particularly in that it points out the absolutely fundamental fact that in all probability the low blood pressure which results from venopressor disequilibrium is not the principal causative factor of shock, as it is so generally assumed, but is rather the direct result of shock. Henderson's main line of thought may be sketched as follows: As a result of various factors—pain, excessive flow of afferent impulses, or exposure of viscera—there is a loss of carbon dioxide either by excessive lung ventilation or by direct exhalation from the viscera. Carbon

¹ Observations upon the Cause of Shock and the Effect upon it of Injections of Sodium Carbonate, Contributions to Medical Research, dedicated to V. Vaughan, 1903.

² A series of Papers on Acapnia and Shock, Amer. Jour. Phys., xxi, 126; xxiii, 345; xxiv, 66; xxv, 310; xxvi, 260; xxvii, 152; Johns Hopkins Bulletin, August, 1910.

³ Changes in Heart Rate and Blood Pressures Resulting from Severe Hemorrhage and Subsequent Infusion of Sodium Bicarbonate, Jour. Exper. Med., 1905, vii, 1.

dioxide is an important though poorly understood regulator (hormone) of many of the vital functions (cardiac, peristaltic, respiratory, venopressor), consequently when the loss of carbon dioxide becomes quantitatively sufficient these vital functions are thrown out of gear up to the point of compromise or further, even to cessation of activity. Contrariwise, balance may be restored by methods adapted to increasing the deficient carbon dioxide content of the blood. Henderson's⁴ views have been vigorously attacked by physiologists, and his own data has been used to disprove his main thesis. But leaving aside all polemic discussion it may be stated fairly that if in accordance with Henderson shock is caused by acapnia or a lessened carbon dioxide content in the blood, then the direct introduction of carbon dioxide into the blood ought to be a powerful and fairly certain remedial agent.

On the above assumption we based the following series of experiments. Before describing our experiments, however, it must be stated that two essential facts were kept constantly in mind, namely: (1) Blood-pressure readings in shocked animals must be interpreted merely as expressing phenomena, coincidental with and not necessarily causative of shock. Attention is centred largely on blood pressure because it is conveniently measurable accurately and graphically, and because, in a sense, it furnishes an index of the degree of shock. (2) In the anesthetized dog there are remarkable spontaneous variations of pressure which, as far as can be determined, have nothing except a coincidental relationship with procedures aimed at either producing or relieving shock. These variations in pressure will necessarily be falsely interpreted unless a large number of control experiments are performed as routine work.⁵

Assuming the correctness of Henderson's assumption that shock is due to a deficiency of carbon dioxide in the circulatory blood, we attempted to check up his theory by supplying the blood stream directly with an increased quantity of this gas. For obvious reasons the demands of accurate experimentation would not be satisfied by infusing a solution of carbon dioxide in water or in an isotonic medium. In our earlier experiments we were deterred from introducing pure carbon dioxide gas into the circulation by the fear of gas emboli, therefore it was determined to use a molecular solution

⁴ Henderson himself attempted to increase the carbon dioxide content of the blood by two methods, both of which are open to criticism. His method of infusing physiologic salt solution saturated with carbon dioxide is open to question on account of the bulk of fluid necessarily injected (Henderson does not furnish figures or details of these infusions) and his method of increasing the dead space of the respiratory tract is open to criticism because it is not accompanied by analysis of the lung and blood gases before and after.

⁵ The conclusions on which this paper is based rest upon a hundred odd experiments performed on forty-six dogs. All the experiments were performed with the animal under profound morphine—Grehant (chloroform) or morphine ether anesthesia. We are deeply indebted to Dr. B. F. May for valuable assistance rendered during the summer of 1911 in a large series of experiments.

of sodium bicarbonate. There are three elements in the blood which split up the sodium bicarbonate molecule and set free carbon dioxide: (1) The hemoglobin; (2) the serum albumin; (3) the primary (acid) sodium phosphate. It will be seen therefore that the introduction of a solution of bicarbonate into the blood stream furnishes a direct and immediate increase of the carbon-dioxide content.

We may say at the outset that, without exception, every infusion of sodium bicarbonate caused a pronounced rise of blood pressure. In our first experiment, in which we introduced intravenously 200 c.c. of an 8.4 per cent. solution, the rise was so remarkably high, so long continued, and so notably in contrast with the efficiency of all the other antishock drugs and procedures that we had tried during the past five years that the practical therapeutical phase of the problem almost overshadowed the purely scientific inquiry regarding the influence of the carbon-dioxide content of the blood. A molecular solution of sodium bicarbonate was injected fifty times under varying conditions of blood pressure. An analysis of the results obtained from this set of experiments furnishes the following facts: (1) When 25 c.c. of the solution is injected into a normal (anesthetized) dog, with normal blood pressure, it occasions no rise of pressure and no perceptible increase of amplitude of beat. When, however, the injection is made into a dog reduced to a state of shock by manipulation and chilling of the abdominal viscera there is an immediate rise of pressure. Quantitatively this rise depends largely upon the age and general condition of the dog (old dogs respond much less vigorously than do young ones) and also upon the degree of shock. In moderate shock the rise is much more pronounced than in the later stages. We consider a rise of 18 mm. (mercury manometer) to be an average effect, but it was not uncommon for an injection to be followed by a rise of 40 mm. It was noted in analyzing our tracings that more significant than the sharp response to the injection is the steadiness with which the blood pressure climbs and maintains itself at a high level. We found in many instances that after the new level of pressure was established it required rough manipulation to reinduce the previous low level of shock pressure, and we believe that those dogs that received an initial injection of sodium bicarbonate before the abdomen was opened and while the pressure was at its normal height were reduced to a state of shock with more difficulty than those animals that did not receive an initial dose. Such a statement of course is difficult of proof because of the varying resistance of different animals to the various manipulations we practised.

Hand in hand with the rise of pressure went an increase of amplitude of heart beat. This increase varied quantitatively as did the rise of pressure itself, its chief characteristic being its constancy. Not infrequently the amplitude of beat was doubled

immediately after the injection of the bicarbonate, and the increased amplitude often persisted for half an hour or longer after the injection of the solution. We were fortunate in encountering one dog (experiment 16) that showed an abnormally large amplitude of beat before shock was induced. In this animal the amplitude of beat was 24 mm. In the state of shock the amplitude fell to 15 mm., but following the injection of 25 c.c. of a molecular solution of sodium bicarbonate the amplitude rose to 21 mm. Likewise in some animals very susceptible to manipulative procedures, with a normal low amplitude, in whom the cardiac weakness was so pronounced as to barely record any systolic-diastolic differences on the tracing the injection of the bicarbonate solution was immediately followed by an amplitude of beat measuring 3, 4, and 5 mm. This increase of amplitude, as we have pointed out in the case of the blood-pressure rise, is also well maintained over a fairly long period of time. One experiment (experiment 19) was particularly instructive in demonstrating the contrasting effects of sodium bicarbonate and adrenalin, one of the stock antishock drugs. The immediate effect of the first adrenalin (1 to 5000) injection was to raise the blood pressure without influencing the low amplitude of beat; following the injection without an appreciable time interval the blood pressure fell to a lower level than before the injection, and at this level it remained. A second injection of a stronger solution of adrenalin (1 to 1000) caused a more marked rise of pressure and a pronounced increase of amplitude lasting one minute, followed by a fall of pressure again to a lower level than before the injection and a diminution of amplitude to its previous small height of 1 mm. At this stage 50 c.c. of a molecular solution of sodium bicarbonate was injected and was followed by a well-sustained rise of pressure and by an increase in amplitude up to 4 mm.

In all of these fifty experiments with sodium bicarbonate we could not determine any effect on the rate of heart beat. When the bicarbonate was administered before shock was induced the rate of beat was not quickened, and when it was administered during the period of rapid heart action incidental to shock the rate was not slowed. These facts tally with the results of Howell⁶ in his study of sodium carbonate.

In addition to its influence on the cardiovascular apparatus the sodium bicarbonate infusions exerted a marked effect on the respiratory function. The rate of respiration was sometimes increased, sometimes slowed, and sometimes unaffected. These variations did not seem to depend upon idiosyncrasies in the different dogs, for we observed all in the same dog following different injections of the same amount of the drug. The notable fact was

⁶ Loc. cit.

that the depth of respiration was increased. This respiratory response which followed almost immediately upon the injection of the salt and persisted for a long period after the injection had been made was so pronounced as to attract attention by the marked thoracic movements and the deep sighing respirations. Graphic tracings were necessary merely as a matter of record. The explanation of the increased respiratory activity undoubtedly rests upon the influence of the excess of carbon dioxide upon the respiratory centre, for the respiratory phenomena observed after the injection of sodium bicarbonate were practically identical with those noted after the injection of pure carbon dioxide gas in later experiments. By using a marked excess of sodium bicarbonate solution the respirations could be made feeble and shallow, and for short periods even inhibited.

Such then were the effects noted upon the cardiovascular and respiratory mechanisms, following the injection of small quantities (25 c.c.) of a molecular sodium bicarbonate solution: marked increase of blood pressure, the increase following immediately upon the start of the injection and being well sustained for varying long periods; no influence upon rate of heart beat; marked increase of amplitude of beat, this increase likewise being well sustained over varying long periods of time; varying effects upon rate of respiration; constant effect upon depth of respiration, which was so increased as to be noticeable without the aid of tambour and drum.

It seemed to be evident after the first experiment that the pressor effect of sodium bicarbonate could hardly be explained on our *a priori* assumption that carbon dioxide was liberated intravascularly, thus replacing the gas lost as a result of shock (acapnia—Henderson). For, as we have already noted, coincidently with the rise of pressure following the injection of the bicarbonate there set in a period of marked and sometimes violent respiratory activity that induced a more thorough and prolonged ventilation of the lungs than we have ever seen caused by procedures planned to cause shock. If Henderson's theory of acapnia were correct such ventilation ought to have deepened the shock of our animals (25 c.c. of our solution contained 2.1 gm. of carbon dioxide gas, which could hardly be a sufficient quantity to make up any marked deficiency in the blood) on account of the marked increase in respiratory activity and resultant pulmonary ventilation. Since therefore the rise of blood pressure could not, with certainty, be explained on the basis of increased carbon dioxide content of the blood, we tried to determine what other factors might be discovered as possible explanations of the pressor effect of sodium bicarbonate. We attacked the problem by the process of exclusion and took up in order the influence of (1) the bulk of fluid injected; (2) hypertonicity of the fluid injected; (3) alkalinity of the fluid injected;

(4) influence of free carbon dioxide (intravascular) on the blood pressure.

BULK OF FLUID INJECTED. It is unquestionably true that the intravascular addition of any appreciable quantity of fluid to a shocked animal will cause a rise of pressure. This rise is usually transitory and the transitoriness usually measures directly to the degree of shock. In the marked grades of shock the fluid escapes into the tissues (edema) about as rapidly as it is introduced into the vessel, and therefore causes slight or no rise of pressure. In order to avoid any confusion of interpretation, such as might arise from mere bulk of fluid injected, we always introduced amounts under 26 c.c. We are therefore in a position to state that the rise of pressure following our injections was not due to mere bulk of fluid. In a number of experiments we noted a distinct rise after the introduction of from 2 to 5 c.c. of a normal solution of sodium bicarbonate. In this connection one series of experiments furnished particularly interesting results: A given quantity of sodium bicarbonate (2.5 grams) was injected into the shocked animals in dilutions of 1 to 10 and 1 to 40. The animals that received a 1 to 10 dilution (that is, 25 c.c.) showed the typical well-sustained rise already described, whereas those that received a 1 to 40 dilution (100 c.c.) showed a much more pronounced initial rise following the injection, with a tendency to sustain the high level. The greater rise caused by the more dilute solutions can be attributed only to the excess of fluid (75 c.c.) introduced, for in both instances the quantity of sodium bicarbonate was the same.

INFLUENCE OF HYPERTONICITY. It has been demonstrated by numerous observers that in shock there is an escape of plasma from the bloodvessels into the tissues. This observation has been confirmed at autopsies and also by the determination of the specific gravity of the blood, which is heightened in shock as a result of concentration of the blood. It has even been suggested that shock is due to increased specific gravity of the blood. If the current of the stream of liquid from the vessels toward the tissues could be reversed, or even stopped, the specific gravity of the blood would not be raised. It is possible that the introduction of a hypertonic solution might accomplish this purpose and that our sodium bicarbonate infusions might have been effective on this basis. That this assumption is not correct, however, we proved by the simple experiment of infusing shocked dogs with the hypertonic salt solution and with hypertonic basic sodium phosphate solutions, with practically no effect on the low blood pressure. Dawson⁷ working with hypertonic sodium bicarbonate solution secured results identical with ours.

⁷ Loc. cit.

INFLUENCE OF ALKALINITY. It is so natural to assume that any phenomenon following the use of an alkaline salt is due to alkalinity that we must guard against a *post hoc* error in logic in explaining the pressor effect of sodium bicarbonate on the basis of its being an alkaline salt. In order to determine the influence of alkaline salts on the low blood pressure of shock, we infused various dogs with small quantities (25 to 50 c.c.) of 0.1 per cent., 0.25 per cent., and 1 per cent. of potassium hydrate in physiologic salt solution, with half molecular solutions of basic sodic phosphate ($\text{Na}_2\text{H.P.O}_4$), with half molecular solutions of sodium carbonate, and with molecular solutions of the alkaline tribasic sodic phosphate. These experiments showed conclusively that alkalinity alone cannot explain the rise in pressure. Sodium carbonate, for example, which is a much more strongly alkaline salt than is sodium bicarbonate, invariably gave a pronouncedly less marked rise of pressure. The basic sodic phosphate in most of our experiments gave no rise of pressure (this basic salt is in reality only slightly alkaline), and when a rise did occur following its use we were unable to determine positively that this rise was not coincidental rather than a casual result. The various solutions of sodic hydrate never caused a rise. The tribasic sodic phosphate, which is a strongly alkaline salt, caused only the slightest rise, and this rise was immediately followed by a fall that in two instances ushered in death.

On the evidence at our command, therefore, we are obliged to conclude that the pressor effect of sodium bicarbonate does not depend solely upon the alkalinity of this salt. This conclusion is important in its bearing on the possible relationship between shock and acidosis, recently emphasized by Henderson. The problem of neutralization of acid by alkali substances in the blood is far from being as simple a problem as it is *in vitro*, as the following experiment demonstrates. By the introduction into the circulation gradually of a normal solution of acid sodic phosphate ($\text{NaH}_2\text{P.O}_4$) the pressure may be influenced just as it is by shock, that is, it falls. If not too much of the salt is introduced the pressure rises again spontaneously, just as it does in a shocked dog that has not been too much compromised. By repeated small injections the pressure may be made to reach a stage where spontaneous recovery does not occur and where to all intents and purposes (at least as far as manometric readings go) the animal is in a state of rather profound shock. The analogy between shock and acidosis seems on the face of it to be strong from this experiment. This analogy is further strengthened by the fact that the injection of a small amount of sodium bicarbonate immediately restores the blood pressure to a marked degree. Spiro⁸ first out-

⁸ Beit. z. Lehre von d. Säurvergiftung bei Hunde und. Kananschen, Hofmeister Beit., 1902, Band i.

lined this experiment as an example of alkaline neutralization of an acid intoxication, and Jacoby⁹ considers the experiment as an evidence of "entgiftung" or neutralization of poisonous acid salt by an alkali. We were able to confirm in detail the experiments of Spiro, but additional experiments performed by us did not point conclusively to the fact that the rise of pressure following the infusion of sodium bicarbonate was solely due to the alkalinity of this salt. For example, if acidosis were induced by infusing the acid sodic phosphate until a steady low blood pressure was reached the pressure could not be raised by instilling 0.25 to 1 per cent. solutions of sodic hydrate; the introduction of the basic sodic phosphate also had practically no effect, and the introduction of the tribasic sodic phosphate was followed by a rise of pressure not comparable either in degree or in duration to that secured by injecting sodic bicarbonate. Of course, this phase of the problem is fogged by the element of the toxicity of both sodic hydrate and the tribasic phosphate; but, nevertheless, we feel safe in assuming that in these acidosis experiments the pressor effect of sodic bicarbonate cannot unquestioningly be referred to its alkalinity alone.

At this point we were forced in spite of our fears of gas emboli to test out the possible blood pressure raising effect of carbon-dioxide gas supplied directly to the blood in shock. Our first experiment demonstrated that we could, with safety, introduce carbon-dioxide gas directly into the femoral vein from a Kipp generator. A detailed study of the physiologic effects of the intravascular injection of carbon dioxide will be made in a subsequent report. It will suffice here merely to say that by properly regulating the flow of gas we could administer it over an indefinite period of time, and that although the administration stimulated the respiratory function most actively it did not influence the rate of heart beat, amplitude of pulse pressure, or height of blood pressure. When the carbon-dioxide gas was administered before shock was instituted it had no influence in warding off the oncoming fall of pressure, and when administered during shock it likewise had no influence in restoring pressure toward a normal level. It would seem to be clearly established therefore both that the pressor effect of sodium bicarbonate does not reside in the carbon dioxide radical, and that shock itself cannot be referred to acapnia.

The direct vasomotor effect of the sodium bicarbonate solution upon the bloodvessels we have not tested out. Howell,¹⁰ in his work upon sodium carbonate (a salt which, as we have seen, is closely allied to the bicarbonate in its action) says: "It is impossible from the experiments to state positively whether or not the

⁹ M. Jacoby, *Einführung in d. Exper. Therapie*, Berlin, 1910, verlag Julius Springer.

¹⁰ Loc. cit.

alkaline injections had any effect upon the tone of the peripheral arteries, but the impression that I have obtained from a study of the records is that they act solely as a stimulant upon the heart and that the increased arterial pressure was due chiefly if not entirely to a more vigorous heart beat."

Since none of the factors of bulk, hypertonicity, alkalinity, or free carbon-dioxide gas showed itself the sole cause of the pressor effect of sodium bicarbonate, we were forced by exclusion to assume that this salt acts specifically upon the heart muscle. This assumption receives corroboration from the fact that with both vagi cut, and even with all the higher cerebral centres destroyed by Jackson's¹¹ method, an injection of sodium bicarbonate is followed by a rise of blood pressure.

PINCHING THE APPENDIX IN THE DIAGNOSIS OF CHRONIC APPENDICITIS.

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NOTHING in medicine in the way of examination seems to have been better learned than McBurney's point and its significance in connection with the diagnosis of appendicitis. It is rare indeed among the students of my postgraduate teaching experience to ask the question "What is McBurney's point?" and not receive an intelligent and capable answer. There is no doubt that the sign is of much value in the diagnosis of appendicitis, but that it fails at times is the purpose of this article.

In the average case of pain in the lower right quadrant of the abdomen, some rise in temperature, increase in the pulse rate, a spasm of the abdominal muscles over the area, and perhaps pain and tightening when the thigh is straightened on the pelvis, the diagnosis is easy. In these cases the area of tenderness upon pressure is so much larger than the area which corresponds to the appendix itself that pressure midway between the umbilicus and superior spine of the ileum in a backward direction serves the purpose. But there are frank cases, usually subacute or those with a small abscess, wherein the tenderness on pressure is lower than would correspond sharply to McBurney's point. In the average person when the head of the cecum is in normal position, an inch or so above the brim of the pelvis, the base or length of the appendix is slightly

¹¹ The Production of Experimental Cephalic Coma, Jour. Pharm. and Exper. Therapy, 1902, vol. iv, No. 1.

outside or midway on the spine and umbilical line, and there are many individuals in whom the cecum is much lower, and in them pressure upon what is McBurney's point may not elicit the tenderness that would come from pressure lower down over what would then correspond to the site of the appendix. This is particularly true in cases of chronic appendicitis where all that may be useful in the way of physical examination is a tenderness localized to the appendix. Not considering those cases that give a history of recurring acute attacks, there are many with dyspeptic symptoms due to a diseased appendix, this usually being a chronic process in which this sign may be important to diagnosis.

In this connection I desire to criticize the teaching of some of the surgeons that appendicular dyspepsia may exist, with no tenderness in the appendix region. It is always fair to the patient that no diagnosis of chronic appendicitis be made in those cases, even when the dyspepsia symptoms have subsided after the appendix had been removed, because it may be that the patient had fears of the appendix being the cause of the dyspepsia and the removal of it acted autosuggestively in a favorable way upon the dyspeptic symptoms. I believe that an appendix must be tender before it can be of significance in causing dyspeptic symptoms.

In the diagnosis of chronic appendicitis we must take into consideration the conditions of Lane's kink, Jackson's, and firmer membranes of the cecum, together with some less well-known conditions, such as insufficiency of the ileocecal valve, chronic excessive intestinal putrefaction causing a tender cecum, mainly at its head, and states connected with the ovary or extracecal structures.

Taking cases with a history of chronic disorder in which more or less distress exists in the right iliac fossa, diagnosis of the above-mentioned states can only be made as follows: Lane's kink by radiographs taken when the bismuth has reached the ileocecal region, these being made with the patient lying on the left or right side and preferably in Trendelenburg's position. The same is true of Jackson's and firmer membranes of the cecum wherein the mobility of the cecum can be studied by the x -rays and the presence of a membrane suspected. In addition to that a careful study of the bacteriology of stools with reference to their anaërobic content suggests the cause of membrane formation, for Jackson's membrane is a protective process in which the endothelium of the peritoneum is raised by a hyaline subendothelial substance, vascularity of the membrane taking place as a nutritive process. Further, the double-barrelled colon is usually accompanied by these membranes.

Insufficiency of the ileocecal valve can only be diagnosticated by the x -rays, with a fluid bismuth suspension being introduced per rectum. The tender cecum due to chronic excessive intestinal

putrefaction is diagnosticated by a careful study of the stools and urine. This means the establishment of the patient on a known diet and the recording of the quality and quantity of foods for several days. Then careful and complete analyses of a twenty-four hour collection of urine and specimens of stool must be made, carrying the first through the sulphate partition, estimating the oxalic and uric acids, and so forth, and the second through the fermentation and putrefaction tests, as well as through the products that such feces manufacture during these tests, with a careful study of the bacteriology.

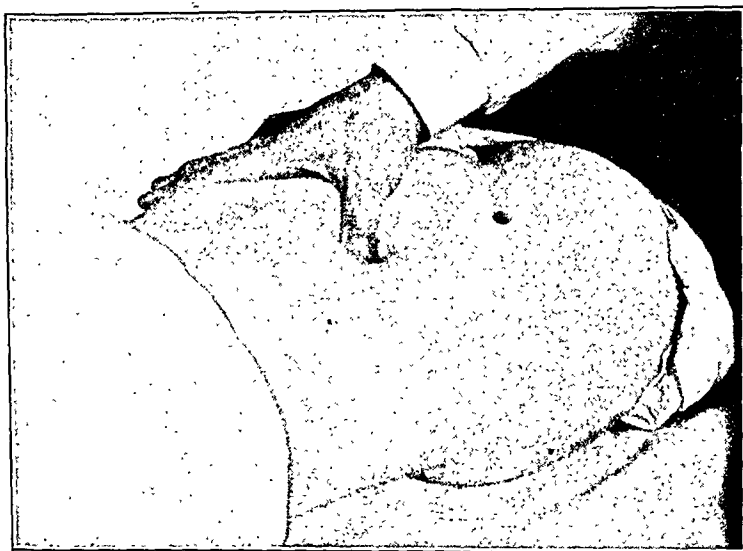
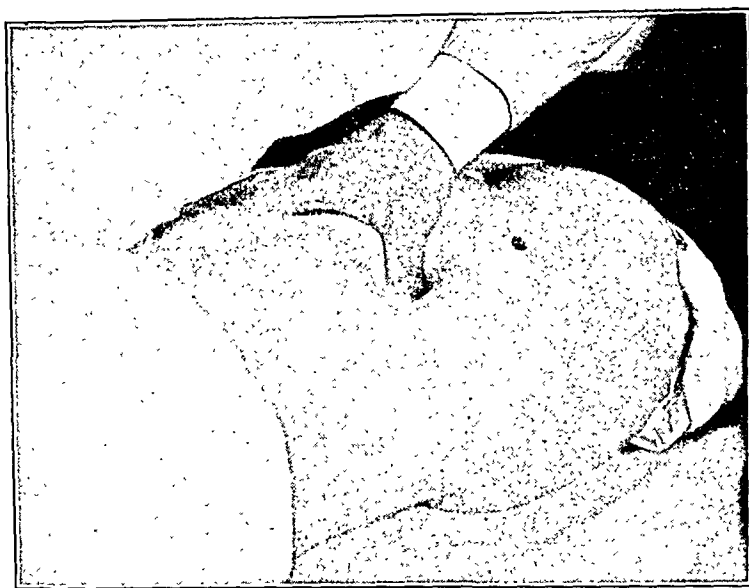
Conditions of the right ovary can usually be excluded by bimanual palpation, provided one is careful in palpating the ovary between the fingers, causing it to slip about on the end of the internal finger. Inflamed or diseased ovaries are tender upon pressure. After the tenderness of the ovary has been elicited the external hand makes pressure at right angles away from the ovary to the lateral wall of the pelvis and in a backward direction toward the appendix. In a simple case it will then be noted that no tenderness exists beyond the ovary.

As was stated before, the appendix may occupy any position from the line drawn from the umbilicus to the anterior superior spine downward to the brim of the pelvis. It is logical that pressure upon McBurney's point in an appendix that is chronically diseased and located below it will not elicit the tenderness that pressure below the point would, and if the subject be a female, one is liable to make the mistake and think that the right ovary is at fault. For the purpose of helping to differentiate this on abdominal examination alone a little extra consideration is required.

Covering the majority of cases met with clinically and in thin subjects a point midway between the anterior superior spine and the umbilicus falls inside of the right edge of the rectus on that side. In the general run of cadavera if a long needle is driven down from this point and then dissection made it will be found that its course corresponds to inside the cecum, considering the cecum on a curved vertical line. In some, in the prone position it is directly over the cecum. Now in these when one makes pressure directly backward, as is done in obtaining McBurney's tenderness, one is liable to press inside of the cecum or upon it and not over the appendix. In a number of appendices that I have had removed I have found the following plan to be decidedly more successful.

If the patient is not too stout the lower border of the cecum is percussed for from Poupart's ligament upward. Fortunately the cecum is usually distended with gas and an accurate level of the cecum when the patient is on the back can be determined. After this is noted, percussion transversely across the cecum is made to obtain its outer and inner edge. The outer edge is always possible of being noted. In percussing for this it is necessary when

on the outer edge that the percussion stroke be directed straight backward toward the lateral edge of the body, and when on the inner, directly backward toward the junction of the psoas and



Pinching the Appendix. First shows pressure on a line midway between the umbilicus and the anterior superior spine of the ileum on the right side, the latter marked with a black dot. The second, the swinging of the thumb to the right of the patient, and pinching the appendix against the iliacus muscle. Patient viewed down the right side, head to the left of photograph.

iliacus muscles at that area—these lines being more oblique than the outer edge of the rectus. With an estimation of about where the appendix would be as judged from the location of the lower end and sides of the cecum, pressure on the abdomen should be

made at that point. When the cecum cannot be mapped out by percussion or the subject is well developed, and even in all, the second plan is to note the position of the right edge of the rectus muscle on the umbilical-spine line maintaining the site with a finger. Having the patient rise to a sitting position helps in palpating for the rectus edge. Standing at the right and facing the patient (for right-handed individuals) the thumb is placed vertical on the abdomen, the tip of the thumb pointing to the ensiform, when it is slowly pressed backward into the abdomen, not inward, outward, up or down. When the thumb has been sunk about half-way down to the back of the abdominal cavity, it is swung to the right of the patient at a right angle to the downward pressure line. This pinches the appendix against the iliacus muscle and unyielding structures under and at the side of it, and usually elicits pain or tenderness. It is well, having done this in the mid-distance between the anterior superior spine and the umbilicus and not having obtained tenderness, to move the thumb down about one-half inch, performing it again, and so on downward until one has reached almost to the brim of the pelvis. The same procedure on the left side serves as a control. By means of this method of downward and then right lateral pressure it is possible to elicit tenderness in the average case of chronic appendicitis. When tenderness is obtained on transverse pressure to the left it may be a Lane's kink, and when below it may be a tender ovary instead of an appendix.

THE EFFECTS OF CONTINUOUS ADMINISTRATION OF EXTRACT OF THE PITUITARY GLAND.

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THE present investigation was undertaken in order to study more particularly the effect of pituitary extract upon the blood pressure when administered by the mouth over a more or less prolonged period, but also, at the same time, to observe other phenomena which might be attributed to the employment of the drug.

The effect of intravenous or hypodermic injections of preparations of the pituitary gland upon the blood pressure has been studied by numerous observers, and the gland has been given *by mouth* for long periods in the treatment of infantilism; but in the first case the observations were only taken for a comparatively short time, and usually after one large or several frequently repeated doses, and in the latter case no systematic studies have been made

of the effect of the prolonged use of the gland upon the blood pressure.

Various observers have shown that injections of extract of the infundibular portion of the pituitary gland cause a rapid and pronounced rise in blood pressure, which persists for a variable time, usually much longer than that produced by adrenalin, and which is due to the constriction of the peripheral arteries. Repeated injections, however, result in a less marked rise in the blood pressure after each injection until finally a fall in pressure occurs. Various theories might be employed to explain this fall:

1. That it is due to a saturation of the blood, with pituitary extract, "so that an interaction takes place which converts its constricting action on the peripheral vessels into a dilating one."¹

2. That it is due to a late depressing action influencing the strength of the cardiac beat.²

3. That it is due to the action of the depressor substance which the gland contains overpowering the pressor substance, causing a dilatation of the peripheral bloodvessels.³

4. That it is due to the central dilator effect of the drug.⁴

5. That there is an inhibitory substance present, preventing a secondary action of the drug.⁵

Of these theories the first and second seem most tenable. It is therefore plausible to attribute the secondary depressor effect of the drug to the larger quantity that is necessary to produce this result. Similar effects are noted with some other drugs which in average dose will produce certain result, while larger, not necessarily lethal doses, will cause a result contrary to the initial finding. In giving fair-sized doses of the glandular extracts by the mouth the overwhelming action of the larger doses is thus obviated and the effects are largely those that result from its primary action. Aside from the action of the infundibular portion of the gland upon the vascular system, several other effects may be observed; thus it has been noted that persistent use of larger doses may cause glycosuria; after single and repeated intravenous injections diuresis occurs; frequently there is a slowing of the pulse rate, perhaps associated with a decrease in the amplitude of cardiac contractions; possibly an inhibition of the flow of pancreatic juice; and usually stimulation of the uterine and intestinal musculature. Clinically, the infundibular portion of the pituitary gland has been extensively employed as an oxytotic, occasionally as a diuretic. It has given

¹ C. P. McCord, An Investigation of the Depressor Action of Pituitary Extracts, Arch. Int. Med., 1911, viii, 609.

² C. J. Wiggers, The Physiology of the Pituitary Gland and the Actions of its Extracts, AMER. JOUR. MED. SCI., 1911, cxli, 502.

³ Schafer and Vincent, The Physiological Effects of the Pituitary Body, Jour. Phys., 1899-1900, xxv, 87.

⁴ T. Sollman, and J. I. Pilcher, Central Vasomotor Effects, Jour. Pharm. Exp. Therap., 1910, i, 571.

⁵ W. W. Hamburger, The Action of Intravenous Injections of Glandular Extracts and other Substances upon the Blood Pressure, Amer. Jour. Phys., 1904, xi, 282.

good results as a vasoconstrictor when employed in the treatment of shock and other conditions associated with transient low blood pressure. It has also been used in many other less relevant conditions. Extracts of the whole gland have been used in the treatment of both acromegaly and infantilism.

In the following series of patients the first few were selected for observation because they had showed persistent low blood pressure upon repeated examination; later, patients showing higher pressures were also given the glandular extract. In all, observations were made upon 18 people, 13 of whom were patients in the dispensary of the Hospital of the University of Pennsylvania, and 5 of whom were medical students who volunteered to assist in the investigation. The extract was given over a period of from one week to ten months without other medication. The 5 students took the extract for only a week, but it was administered to all the patients for at least a month unless stopped on account of some untoward effect. The preparation employed was the extract of the whole gland made up in 0.2 gram tablets containing 0.065 gram of the dried gland, equivalent to 0.26 gram of the fresh gland. The dosage at first was two of these tablets twice a day, but no effect was noted until the dose was increased to one tablet four times a day. Larger doses were given to several individuals, but soon discontinued.

Although most observers have agreed that the posterior lobe or infundibular portion of the gland elaborates the secretion that acts upon the bloodvessels, nevertheless in a recent work, D. Lewis, J. L. Miller, and S. A. Matthews⁶ found that extracts of the *pars intermedia* caused a decided rise in blood pressure, the extracts of the *pars nervosa* also caused an eventual rise in the pressure, as did likewise in the majority of instances, extracts of the anterior lobe. They believe that the pressor substance is secreted by the *pars intermedia* and those cells of the anterior lobe which bound the cleft. It therefore seemed feasible to employ the whole gland not only because of the impossibility of securing preparations containing only the *pars intermedia*, but also because the dried extract is more suitable to prescribe to dispensary patients.

The blood pressure was taken one or more times before giving the pituitary tablets, and then later at each subsequent visit to the dispensary until the observations were discontinued. The blood-pressure readings were all taken two or more hours after ingestion of the glandular extract and after half-hour or more rest in the dispensary. The readings were made by the auscultatory method, systolic and diastolic pressure being recorded while using a Stanton sphygmomanometer.

PATIENT 1.—The glandular extract caused a rise in pressure from 12 to 20 mm. of mercury in all the many observations. The

⁶ The Effects on Blood Pressure of Intravenous Injections of Extracts of the Various Anatomic Components of the Hypophysis, *Arch. Int. Med.*, 1911, vii, 785.

pulse pressure showed but little variation. The pulse rate averaged consistently about 80 beats per minute, except at one time when it fell to 60, after taking larger doses, six tablets a day, for several days. This larger amount also caused diarrhea. Twelve days after cessation of treatment, pressure showed but slight change, in nineteen days it had returned to its former level.

PATIENT 2.—The systolic pressure increased 18 mm. of mercury. The diastolic pressure was unchanged. Diuresis was observed.

PATIENT 3.—The systolic pressure was increased from 9 to 20 mm. at different observations. The pulse pressure was unchanged. A slowing of the pulse rate—60 per minute—was also noted for a short time. At one time during the experiment the patient stopped the drug for six days without any effect on the blood pressure. Eight days after the complete cessation of ingestion of the glandular extract the systolic pressure had returned to within 8 mm. of mercury of the average pressure before the experiment, and in thirteen days had fallen back to the previous average pressure.

PATIENT 4.—The systolic pressure increased 8 to 10 mm. at various observations. The pulse pressure remained unchanged.

PATIENT 5. The increase of systolic pressure varied between 12 and 18 mm. The pulse pressure was unchanged, and the pulse rate was variable.

PATIENT 6.—The increase in systolic pressure varied between 13 and 20 mm. The pulse pressure before taking the gland was 35; during its administration it was between 45 and 65, and the pulse rate averaged 86.

PATIENT 7.—The systolic pressure increase averaged 16 mm. The pulse pressure was unchanged. Diarrhea developed after taking the gland extract for two weeks, and it was therefore discontinued.

PATIENT 8.—This patient suffering with chronic nephritis and low blood pressure was one of the few patients decidedly improved by the action of the gland. The systolic pressure estimated several times before taking the preparation never exceeded 105 mm. of mercury. It rose a short time after the use of the extract to 112; two days later it rose to 120, and henceforth varied between 120 and 125. The diastolic pressure rose synchronously with the systolic. The secretion of urine was decidedly increased, according to the report of the patient, and the subjective symptoms were also markedly alleviated, so that he felt better than at any time during the past several years. The pulse rate also showed an increase, rising from 64 to 92 beats per minute. One week after discontinuation of the drug the pressure was 115 and in two weeks back to 105.

PATIENT 9.—This patient, with a more elevated pressure than the majority of the individuals studied, showed in nine days an increase in pressure equal to 27 mm. of mercury, the pressure

rising to 155 systolic and 90 diastolic. The pulse rate increased to 106. The pituitary extract was immediately stopped.

PATIENT 10.—This patient showed an increase of systolic pressure of 20 mm., but as a severe diarrhea developed the treatment was discontinued.

PATIENT 11.—The systolic pressure was increased, the increase ranging between 12 and 20 mm. of mercury. The pulse pressure ratio remained unchanged. Two weeks after cessation of the drug the systolic pressure had returned to previous figures.

PATIENT 12.—The increase of systolic pressure varied between 15 and 20 mm. of mercury. The diastolic pressure did not show a corresponding increase. The pulse rate was also increased, averaging about 95 beats per minute. Two days after stopping the drug the systolic pressure was down 5 mm. In twelve days it was 5 mm. higher than before starting the experiment. Eighteen days it was approximately at the same level as at the beginning of the drug treatment.

PATIENT 13.—The blood pressure increased from 123 systolic (70 diastolic) to 135 systolic (80 diastolic) in twelve days, when the treatment was stopped on account of diarrhea. The pulse rate increased 15 beats per minute.

Subsequent observations after discontinuation of pituitary extract in these patients showed a tendency for the pressure to return to its previous level after a lapse of about two weeks. This fall occurred gradually so far as could be determined.

Five students took the glandular extract for a week. Four showed a rise in systolic pressure of 4, 10, 15 and 17 mm. of mercury respectively without a corresponding rise in diastolic pressure. One showed no change in the systolic or diastolic pressure. In two of these men no change in the pulse rate occurred, while in the other three there was an increase of 10, 10, and 20 beats per minute. Three noted diuresis; the two that did not note this effect had a rise of 4 and 17 mm. respectively. One man had a slight diarrhea, while 2 had a severe diarrhea, which was worse in the man whose pressure went up the most. Examinations of the urine of the 18 patients were made, and at no time was sugar demonstrated by Fehling's test.

RECAPITULATION. Eighteen individuals were given the dried extract of the whole pituitary gland without other medication. The following effects were noted:

1. Blood pressure: Seventeen showed a rise in systolic blood pressure, the greatest rise being 28 mm. of mercury. Usually a corresponding rise in diastolic pressure occurred, though rarely it remained at the same height as before taking the extract or even became lower.

2. Pulse rate: The changes in the pulse rate were inconstant; an increase was generally observed, though in 2 individuals the rate was decidedly decreased.

3. Diuresis: Six individuals noted a diuretic effect. The extent, absence, or presence of this symptom could not be accurately determined. The urine showed no particular change except in one case (8). Glycosuria was never observed.

4. Intestinal tract: Diarrhea developed in 7 cases, and 4, previously costive, had daily movements during the period of taking the drug.

5. Subjective symptoms: Four individuals were apparently much benefited by the rise in pressure and general stimulative effect of the glandular extract upon the unstriated muscle, and one person was benefited through the diuretic effect of the extract. In the remaining patients there was little effect noted except by those who developed the rather annoying diarrhea.

CONCLUSION. Prolonged administration of extracts of the pituitary gland exert a distinct pressor effect upon the peripheral vascular apparatus, which persists for an appreciable time after discontinuation of the drug. This is apparently the only consistent affect following continued administration of the gland *per oram*; other results are variable and indefinite.

TUBERCULIN THERAPY IN SURGICAL TUBERCULOSIS, WITH THE CORRECT DOSAGE ACCURATELY DETERMINED BY THE CUTANEOUS REACTION.

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IN 1910 White and Van Norman¹ reported a method of determining, by means of a cutaneous reaction, the correct therapeutic dosage of tuberculin for subcutaneous injection. The method was adopted in the surgical and gynecological wards of St. Francis Hospital, Pittsburgh, and has been followed in the treatment of twenty-eight cases of surgical tuberculosis. A more recent article² by the same writers confirms their previous work.

Starting with the theory that much of the benefit derived from tuberculin therapy is due to the reaction on the part of the body cells produced by tuberculin rather than to an induced tolerance to it, the method is based on the variation in susceptibility of different individuals to the action of tuberculin on the skin and when injected into the tissues. The optimum dose, as determined by this method, is the quantity of tuberculin required to produce the greatest local, general, and focal reaction without producing constitutional symptoms, such as rise of temperature, malaise, and other evidences of overdosage.

The dose for each individual is determined according to that

¹ Arch. Int. Med., 1910, vi, 449.

² Ibid., 1912, ix, 114.

individual's susceptibility to tuberculin as shown by the cutaneous reaction, and treatment is begun with this optimum dose instead of starting with a very small arbitrary quantity of tuberculin and gradually increasing the dosage in order to produce a tolerance, as is commonly done in the various methods of tuberculin therapy in vogue today. By the new method the treatment is begun with larger quantities of tuberculin, a longer interval is allowed to elapse between doses, and no effort is made to produce a tolerance. In this way treatment may be continued for months without necessity for changing the dosage.

In our cases tuberculin was used as an adjunct to the usual hygienic and dietetic measures such as rest, fresh air, sunshine, and nourishing food. Sinuses were treated locally, with tincture of iodine or with injections of Bismuth paste. In cases with joint involvement, fixation and extension were employed. Operative treatment was conducted when thought to be indicated, and tuberculin was used after incomplete removal of diseased tissues. In children, operative procedures were limited as much as possible, and consisted chiefly of incision or aspiration of abscesses, and curettement of sinuses. The majority of the cases of tuberculous adenitis in children presented sinuses or broken-down fluctuating glands, which were incised. These patients were treated with tuberculin without removal of the glands. As a rule, tuberculin was not given in cases with temperature above 100°. The hospital patients were treated outdoors, and confined to bed during the febrile period of the disease. Many of the afebrile cases were treated in the out-patient department, with instructions as to their mode of life at home.

The cases were treated until all symptoms disappeared and they were apparently well. An effort was made to continue with the administration of tuberculin for months after there was apparent cure, and this was done in a few of the cases; but in the majority of instances the patients failed to return for further treatment after the disappearance of signs and symptoms.

The diagnosis of the cases was based on the clinical history, physical examination, tuberculin test, x-ray pictures, negative bacteriologic findings in cases with pus which had not been exposed to secondary infection by the spontaneous rupture of the abscess, and was confirmed in a large proportion of the cases by microscopic examination of the tissues removed. The Wassermann reaction was used in some of the cases to aid in excluding syphilis, especially in those cases showing multiple bone lesions.

TECHNIQUE. White and Van Norman³ showed that the quantity of tuberculin required to produce a reaction of 4 mm. on the skin, their so-called "minimal cutaneous reaction," will, when injected intradermically, produce a local reaction at the site of injection 2 to 5 cm. in diameter. They consider this quantity to be the

³ Loc. cit.

optimum dose—that is, the dose that will produce the most marked reaction without producing constitutional symptoms. For determining this dose the technique employed in this series has been practically that advocated by the originators of the method, with a few minor exceptions.

The tuberculin used was Koch's O. T., in various dilutions. In addition to this a von Pirquet scarifier, a pipet which measures $\frac{1}{100}$ c.c. of the tuberculin dilution, and shields for the protection of the site of the skin test were used. For the latter purpose lids of pill boxes, secured in place by strips of adhesive plaster, were found to be sufficient.

On the mesial anterior surface of the forearm the skin is cleansed with ether, and two points, about one inch apart, are scarified by a rotary motion of the scarifier until sufficient epidermis is removed to leave a pink base from which neither blood nor serum exudes.

These scarified areas measure 2 mm. in diameter. The lower area is used as a control, while on the upper area there is placed $\frac{1}{100}$ c.c. of the tuberculin dilution, the shield is applied and the patient is instructed to hold the arm horizontally until the solution dries, which requires twenty to thirty minutes as a rule. The shield is worn until the first reading is made. The readings are made in twenty-four, forty-eight, and seventy-two hours after the tuberculin is applied, and the area of redness and swelling is measured in millimeters.

Since many of the minimal cutaneous reactions (4 mm. in diameter) occur with dilutions near 1 per cent. this dilution serves as a good working basis with which to begin, and thereafter weaker or stronger solutions can be used according to the size of the reaction obtained. For example, if $\frac{1}{100}$ c.c. of 1 per cent. tuberculin produces a reaction 6 mm. in diameter in forty-eight or seventy-two hours, weaker solutions as $\frac{1}{2}$ per cent. or $\frac{1}{4}$ per cent. should be used until a 4 mm. reaction is obtained. The quantity of tuberculin in $\frac{1}{100}$ c.c. of the dilution used to produce the 4 mm. reaction, which quantity, in the case of 1 per cent. tuberculin, would be $\frac{1}{10000}$ gm., or $\frac{1}{10}$ mg., is the optimum dose. This quantity, when injected into the skin, should produce a local reaction 2 cm. to 5 cm. in diameter at the site of the injection, which local reaction serves as a control of the test.

The therapeutic injections were given into the arm every two weeks. No effort was made to inject the tuberculin with reference to the lymphatics in the region of the tuberculous focus, as suggested by White and Van Norman.

REMARKS ON TECHNIQUE.—Until one becomes accustomed to reading the skin reactions it is well, after first obtaining the 4 mm. reaction, to repeat the test with a weaker solution. For example, if a 4 mm. reaction is obtained with 1 per cent. solution the test should be repeated with $\frac{1}{2}$ per cent. solution, and if the previous reading was correct the size of this last reaction should be less than

4 mm. in diameter. White and Van Norman advise waiting three or 4 days between each skin test, and one week after the last skin test before injecting the therapeutic dose. We have, up to the present time, experienced no untoward results with the method, although we have repeated the tests as soon as the readings were made, thus shortening the time required for estimating the optimum dose. Two or three tests are usually sufficient.

Our dilution for therapeutic injections were made so that $\frac{1}{2}$ c.c. contained the desired quantity of tuberculin, thus making a constant bulk of solution for injection in every case.

As the injection into the skin is more painful than into the subcutaneous tissues we have been injecting only the initial dose into the skin. This is done in order to determine the size of the local reaction, which we use as a control of the skin test. The subsequent injections of tuberculin were made into the subcutaneous tissues, except that every two or three months we injected again into the skin to note whether the size of the local reaction had changed, thus determining whether it was necessary to repeat the skin test and estimate a new dose. We have not found it necessary to change the dosage in any of our cases which were treated uninterruptedly. Although some of them were treated over a period of months the local reaction at the site of injection did not vary in this beyond the limits of 2 cm. and 5 cm.

That susceptibility to tuberculin does change was shown in our cases of tuberculous peritonitis, especially when rapid and marked improvement took place after operation. While these cases responded mildly to the von Pirquet test before operation, their rapid improvement after operation was accompanied by a marked increase in the intensity of the reaction to the test. If the dose of tuberculin had been estimated and injected before operation we are unable to say whether this change in susceptibility after improvement took place would have necessitated a change in dosage, as treatment was begun in our cases after operation and not until the patient's temperature had fallen to below 100° , and the general condition was much improved as a result of operation.

For measuring $\frac{1}{100}$ c.c. we use a capillary pipette. One one-hundredth gram of distilled water is weighed on a chemical balance; this quantity of fluid readily passes up the tube by capillary attraction and the upper level is marked. A rubber tube, such as is used on a blood pipette, is attached to the capillary pipette, and with this the tuberculin can be accurately transferred to the scarified area.

The dilutions of tuberculin are made on the basis that 1 c.c. of Koch's O. T. contains 1000 mg., or 100 per cent. of tuberculin. From this, weaker solutions are made with normal salt solution containing 0.25 per cent. phenol. Fresh solutions are made up every two months, and are kept on ice. We keep the following dilutions for the skin test, viz: 10 per cent., 1 per cent., and 0.1 per

cent., and from these 3 per cent. or 0.5 per cent. or any required dilution for the skin test can be made. The solutions for therapeutic injection are made so that $\frac{1}{2}$ c.c. contains the desired quantity of tuberculin. For example:

(a) 1 c.c. of 0.1 per cent. solution plus 9 c.c. diluent— $\frac{1}{2}$ c.c. contains 0.00005 gm. of tuberculin.

(b) 1 c.c. of (a) plus 9 c.c. diluent— $\frac{1}{2}$ c.c. contains 0.000005 gm.

(c) 2 c.c. of 0.1 per cent. solution plus 9 c.c. diluent— $\frac{1}{2}$ c.c. contains 0.0001 gm.

(d) 1 c.c. of (c) plus 9 c.c. diluent— $\frac{1}{2}$ c.c. contains 0.00001 gm.

In this way any dilution can be readily made.

RESULTS.—There were twenty-eight cases treated in this series, consisting of tuberculosis of the kidney and ureter, peritoneum, bones, joints, glands, and skin, as follows:

Case No.	Age.	Tuberculosis of	Operation.	Dose, grams.	Duration of treatment.	Results.
1	29	Kidney and ureter	1. Incision of abscess	.000005	9 months	Well.
18	20	Peritoneum	2. Nephrectomy	.00005	3 months	Improved.
4	46	Peritoneum and pleura	Laparotomy; double salpingectomy	.0001	1 month	Well.
			1. Thoracentesis; paracentesis			
			2. Laparotomy; appendectomy			
16	3	Inguinal glands	None	.00001	3½ months	Well.
23	16	Axillary glands	None	.00002	2 months	Improved.
						Under treatment now.
19	4	Cervical glands	None	.00005	3 months	Improved.
20	23	Cervical glands	None	.0001	3½ months	Improved.
26	16	Cervical glands	None	.00001	1 month	Under treatment.
27	3	Cervical glands	None	.00002	2 weeks	Under treatment.
9	26	Cervical glands	Incision of abscess	.00005	2½ months	Improved.
12	17	Cervical glands	Excision of glands (incomplete)	.00001	3 months	Well.
13	18	Cervical glands	Excision of glands (incomplete)	.000005	2 months	Improved under treatment.
22	29	Cervical glands and lungs	None	.0001	3 weeks	Unimproved.
15	2	Cervical glands and hip	Aspiration of abscess—hip	.000005	2 months	Well.
28	4	Cervical and inguinal glands	Incision of abscess—neck	.00002	2 weeks	Under treatment.
10	7	Cervical glands and bones (multiple)	Incision of abscess—neck and curetment of bone sinuses	.00001	3 months	Improved under treatment.
11	2½	Bones (multiple)	Curetment of sinuses	.000005	2 months	Improved under treatment.
14	7	Bones (multiple)	Curetment of sinuses	.00001	3½ months	Improved.
6	35	Bones (vertebræ)	Laminectomy	.00005	7½ months	Dead.
3	16	Hip	None	.00015	1½ months	Well.
25	10	Hip	None	.00005	2 months	Improved under treatment.
5	42	Hip	Incision of abscess	.00005	5 months	Well.
8	6	Hip	Aspiration of abscess	.00005	2½ months	Well.
24	2	Knee	None	.00005	2 weeks	Unimproved.
2	39	Ankle	Arthrotomy and curetment	.00005	1 month	Improved.
7	5	Ankle	None	.00001	8½ months	Well.
17	30	Elbow	Resection of joint	.00005	1½ months	Well.
21	16	Skin	None	.00001	5 months	Well.

Ten of these were aged above and 18 below twenty years, 11 of the latter being under ten years and the remaining 7 between sixteen and twenty years. The dosage of tuberculin in this series varied from $\frac{1}{200}$ mg. to $\frac{1}{2}$ mg., showing a variation in susceptibility of a hundred fold.

In the 10 cases above twenty years of age the dosage varied from $\frac{1}{20}$ to $\frac{1}{10}$ mg. in 8 of them. In 1 case it was $\frac{1}{200}$ mg., and in the other it was $\frac{1}{2}$ mg., which was the largest estimated dose in the series. This patient was aged twenty years.

Of the cases below twenty years the dosage was $\frac{1}{200}$ mg. in 3, $\frac{1}{100}$ mg. in 7, $\frac{1}{50}$ mg. in 3, $\frac{1}{20}$ mg. in 4, and $\frac{3}{20}$ mg. in 1.

In a general way the dosage below twenty years of age was near $\frac{1}{100}$ mg., while above twenty years of age it was near $\frac{1}{15}$ mg. This emphasizes the increased susceptibility to tuberculin of younger individuals. On the other hand the variations and exceptions, as in the case of the one patient above twenty years of age, for whom the dose was $\frac{1}{200}$ mg., shows the value of a method whereby the dosage is determined according to the individual susceptibility of the patient to tuberculin.

The longest time during which any one patient was treated was nine months. 3 patients were treated for periods extending over seven months. In none of these was it necessary to change the dosage as originally determined by the skin test. There was noted from time to time a variation in the size of reaction produced at the site of injection, but this variation was between 2 cm. and 5 cm., which are the arbitrary limits of the size of reaction that should be obtained at the place of injection.

In 3 cases (10, 11, and 13) who stopped treatment before they were discharged, and who later returned for further treatment after intervals of nine to eleven months, it is interesting to note that the dosage remained the same.

The method of determining the dose has been found reliable in all cases. Constitutional symptoms were obtained in 1 case (11), but through no fault of the method. In this case a reaction of 6 mm. was obtained with $\frac{1}{50}$ mg. of tuberculin on the skin. As there was not sufficient time to do another test before the next regular day for therapeutic injections, $\frac{1}{100}$ mg. was assumed to be the quantity that would produce a 4 mm. reaction. The injection of this quantity was followed by constitutional symptoms. Later, $\frac{1}{200}$ mg. was found to be the correct dose as determined by the skin test, and was given without producing constitutional symptoms.

Of the 28 cases, 11 are considered as well, 11 improved, 5 unimproved, and 1 dead. As will be seen farther on, the 5 unimproved cases were treated for too short a time to be considered in estimating the value of the method from the standpoint of end results. Of the 11 cases discharged as well, 7 returned recently for examination and have remained well as follows:

Case 1, twelve months after discharge.

Case 3, nineteen months after discharge.

Case 4, twenty months after discharge.

Case 5, sixteen months after discharge.

Case 7, eight months after discharge.

Case 16, three and a half months after discharge.

Case 21, one and a half months after discharge.

The remaining 4 were discharged as well, and have not been heard from since then.

One of the chief difficulties experienced has been to get the patients to return for treatment after the visible lesions have healed. Cases with a sinus, as in cervical adenitis, were treated until the sinus healed, when frequently the patient would fail to return for further treatment, although other enlarged glands might be present. These cases have been designated as improved.

Of the 11 cases improved, 2 (9 and 19) were cases of cervical adenitis, with sinuses, who, after the sinuses were healed, failed to return for treatment, and have not been heard from since. Two cases (10 and 13) of cervical adenitis who discontinued the treatment after the sinuses were closed, returned later with recurrence, and are at present under treatment. One case (20), with enlarged glands of neck without sinus, failed to return after the tenderness had disappeared. One case (23) had involvement of the axillary glands, with sinus. The sinus is now healed and the patient is still under treatment. Case 25, with tuberculosis of the hip, is apparently well and is still under treatment. Four cases (2, 11, 14, and 18) have discharging sinuses which were definitely improved, but for various reasons these patients did not continue treatment. Two of them have not been heard from, and another (11) returned later and is at present under treatment. The other was almost healed when he left, and has written recently that the sinuses are healed.

Of the cases marked as unimproved, 1 (25) received one injection, and 1 (22) received two injections and did not return for further treatment. 2 (27 and 28) have received one injection and 1 (26) received two injections, and are still under treatment. These cases are reported not for the final results, but because the dosage was determined by the method described above.

The 1 case (6) with Pott's disease which died, showed marked improvement symptomatically and in his general condition for two months, when he suddenly developed paraplegia and died eight months later. With this one exception all cases treated have been cured or improved, as the cases marked unimproved were treated for too short a time to be considered in the end results.

Many of the cases with sinuses which previously had been treated for months without improvement showed rapid improvement after the tuberculin injections were begun. This happened frequently

enough to be more than a coincidence, and we believe, from our experience with this series of cases that tuberculin in doses determined by this method is a valuable aid in the treatment of surgical tuberculosis.

CONCLUSIONS.—1. The variation in susceptibility of different individuals to the action of tuberculin is marked.

2. The correct therapeutic dose of tuberculin for any individual can be determined accurately by the cutaneous reaction.

3. Tuberculin therapy by this method is a valuable aid in the treatment of surgical tuberculosis.

The writer desires to express his gratitude to Drs. R. T. Miller, Jr., and R. R. Huggins, in whose services these cases were treated, for the privilege of reporting the same, and to Drs. White and Van Norman, of the Tuberculosis League of Pittsburg, for their valuable suggestions and aid.

NOTE.—Since this paper was written the dose has been determined by the above method and given without producing constitutional symptoms in two cases, viz., tuberculosis of the cervical glands and tuberculosis of the hip, making a total of 30 cases.

THE INFLUENCE ON GASTRIC SECRETION OF ASEPTIC FOREIGN BODIES IN THE GALL-BLADDER.

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(From the William Pepper Laboratory of Clinical Medicine.)

THESE experiments were undertaken in the hope of finding some explanation for the gastric hyperacidity so frequently found clinically in association with cholelithiasis. As originally planned they formed part of an extensive series dealing with this subject, but before the work was completed, Lichty's¹ work on the same subject and covering the same ground appeared, thus rendering unnecessary their further prosecution. It seems worth while, however, to report the results obtained in the first simple phase of the investigation, partly because they are not in general in accord with those of Lichty and partly because they control possible sources of error in his work. These are the use of the stomach-tube in feeding the animals, the administration of food at irregular intervals, and the brief postoperative period of observation.

¹ The Relation of Disease of the Gall-bladder and Biliary Ducts to the Gastric Functions, AMER. JOUR. MED. SCI., January, 1911, vol. cxli, No. 1.

Lichty's conclusions are briefly as follow: (1) That a lesion of the gall-bladder and ducts may disturb the gastric function. (2) This disturbance most frequently consists of a hypersecretion of gastric juice and a diminution of gastric motility. (3) So-called hyperchlorhydria, with its accompanying symptoms, should be looked upon as an evidence of some definite pathological lesion somewhere in the gastro-intestinal tract or its appendages.

METHODS. The essential feature of the experiment was to place in the gall-bladder with as little trauma as possible a more or less smooth sterile object, too large to enter the ducts, and after appropriate intervals to study the gastric secretion. The details follow:

In the preliminary control period a series of dogs under similar conditions of environment were fed daily, after fasting at least twelve hours, a uniform test meal consisting of one dog biscuit and 50 c.c. of water. The gastric contents were removed forty minutes later and examined by the usual methods of the clinical laboratory. A sufficient number of test meals were given to secure a reliable average figure for each dog individually. Then under complete ether anesthesia the gall-bladder was opened, a sterile round pebble introduced, and the gall-bladder carefully closed again. A month was allowed to elapse in order to exclude immediate post-operative effects, and at the end of that time the gastric contents were studied, at intervals, for six weeks to eight months, and in one dog as long as eleven months, under the same conditions as before operation. The periods of observation were ten days in length, with daily examination. A control animal was at hand and was similarly studied from time to time. After the last period the dogs were chloroformed and the gall-bladder, stomach, and pancreas examined.

This technique it was found could be very easily carried out. Dog biscuit was chosen because after they were accustomed to it the majority of the dogs would eat it readily, though, as a rule, a preliminary fasting of twenty-four hours was necessary before they could be induced to take the first meal. The dogs preferred the dry ground-up biscuits, which they devoured first, drinking the water afterward. Occasionally difficulty was experienced in persuading a dog to take this meal, but as the method seemed in every way preferable to that of Lichty, that is, introducing the meal through a stomach-tube, it was adhered to in all instances. The dogs were kept quietly in their cages after the test meal for forty minutes and the contents then removed by stomach-tube. The passage of a stomach-tube in a dog is very simple if the animal is properly gagged the first few times, after which with most dogs it can be performed without a gag by merely placing two fingers between the teeth alongside the tube. No effort was made to completely empty the stomach by lavage, as this was found to be very difficult if not impossible. In all about 300 test meals

were removed and examined. The first hundred gastric contents obtained were examined in full, but subsequently only the free hydrochloric acid and the total acidity were estimated.

Five dogs were used, one of which was kept as control. The other four returned after operation to apparently perfect health and were studied for varying periods, one for only six weeks, two for eight months, and one for eleven months. At the autopsy on each of these four the foreign body was found in a gall-bladder, which was much shrunk and had greatly thickened walls, but showed no evidence of infection. Microscopic sections of the gall-bladder, stomach, and pancreas showed no significant changes.

RESULTS. The gastric analyses showed no changes as the result of the experimental procedure. (See Table.) In two animals the average acidity after operation was higher than before, while in the other two the reverse was true. In all the animals, both before and after operation, the averages for free hydrochloric acid lay between the figures 16 and 24.6. The figures obtained with Dog I will serve as an example. Before operation 20 satisfactory gastric contents were recovered, with an average figure for free hydrochloric acid of 22.9. Five weeks after operation a series of nine meals gave an average of 20.1, three months after operation a series of ten meals gave 18.6, while eleven months after operation ten meals gave 21.9. The general postoperative average was 19.8. The difference between this and 22.9 is obviously too slight to be significant.

Dog	I	V	VIII	X	XII (control) ²
Average before operation . . .	22.9	16	23	24.6	18.1
Average after operation . . .	19.8	21.3	19.2	15	24.1

The motility of the stomach did not seem in any instance to have been influenced by the experiment, although Lichty found retention in some of his cases.

I wish to express my thanks to Dr. Floyd E. Keene for his performance of the operations.

CONCLUSION. 1. For the study of gastric secretion in dogs repeated test meals (eight to ten must be given).

2. The test meal can be fed by mouth, which is preferable to administering it by tube.

3. The introduction of a sterile pebble into the gall-bladder of the dog caused no change in the gastric secretion or digestion or in the morphology of the stomach or pancreas within a period of eleven months after its introduction.

² Not operated on, but studied at corresponding times.

CONGENITAL BILATERAL FISTULÆ OF THE LOWER LIP.

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CONGENITAL bilateral fistulæ of the lower lip occur so infrequently and the causative factors in their production are so slightly understood that the report of a case and a review of the literature seem to be timely.

After a careful search I was able to find but 22 reported cases, my own making 23 in all.

O. H., male, aged three years. There is no member of the family who, so far as is known, has had any facial or other congenital deformity. The mother and father are normal individuals. No history of syphilis. The child is well.

The photograph shows the fistulæ as they open on either side of the middle line of the lip. There is a slight puckering of the mucosa, forming an oval in the centre, of which there is a small opening which will just admit a probe point. The tract then runs downward and inward toward the median line, and the fistulæ end in blind pockets just under the mucous membrane of the lip on the inner surface. The entire length of each fistula is about 1.5 cm. These fistulæ do not communicate, but at the terminal portion, which lies near the inner side of the lip, they are separated by a thin partition, probably of fibrous tissue. The openings of the fistulæ are filled with a glairy secretion, which is transparent, and when this is wiped away returns in a few minutes. As it does not give the child much trouble, excision at this time is not permitted.

The first observation of this condition was made in France by Demarquay¹ in 1845. Demarquay saw a mother and child, and in each there was a similar condition—harelip, cleft palate, and bilateral fistulæ in the lower lip. No microscopic examination of the tissue taken from the fistulous tract was made, and he concluded that the condition in the lower lip was due to abnormally developed, hypertrophic follicles.

In 1858 Beraud² described similar deformities in a case and in 1860 Murray³ saw four cases in one family and found many other congenital deformities in other members of the same family. Murray thought the condition due to some intra-uterine disease of the mucous glands in the lip.

Richet⁴ saw a grandmother and mother and child in which the condition of bilateral fistulæ of the lower lip was present. Two

¹ Gazette méd., 1845, pp. 52 and 1868.

² Gaz. des Hôp., 1861, No. 73, p. 291.

³ British and Foreign Med. and Surg. Rev., October, 1860.

⁴ Gaz. des Hôp., 1861, p. 174.

of these cases had been published earlier by Demarquay. Richet also saw several cases in a family in which there were other congenital anomalies in other members of the family. Those who had fistulæ of the lower lip had no harelip.

Rose, in Zurich,⁵ reported a case with division of the lower lip and prolongation of the divided sides. In the ends of the two prolonged halves of the lower lip were fistulous openings, one in each side. Each opening led into a tract about 2 cm. in depth, which secreted a clear fluid. Ahlfield credits Rose with three other cases.

Madelung⁶ saw a child, aged one month old, with harelip and cleft palate, and while the contour of the lower lip was normal there were present two tiny teats symmetrically placed one on either side of the middle line of the lip and puckering the mucous membrane of the lip. On squeezing the lip a clear fluid could be expressed. It was not possible to prove the existence of fistulæ with the sound, but excised portions showed, on microscopic examination, the presence of canals. These canals were lined with mucous membrane covered with epithelium and large, pointed papillæ, which differentiated it from the normal mucosa of the lip. On sagittal section muscle fiber was found on the side toward the inner aspect of the lip. These fibers ran parallel to the fibers of the orbicularis oris. On the side of the canal toward the skin no corresponding muscle fibers were found. There was therefore no structure resembling a sphincter.

Zeller,⁷ in 1888, saw a case in von Bergmann's clinic, and collected all previously reported cases. There were 18 cases in all, including his own, 12 of which were accompanied by double harelip, 2 with single harelip, in 2 cases it was not stated, and in 2 cases the fistulæ of the lower lip were unaccompanied by any other congenital deformity. After exhaustive study of the embryologic and morphologic data he concludes that congenital fistulæ of the lower lip are the remains of the fetal furrows in the inferior maxilla, due to amniotic adhesions.

Zeller's reasoning is as follows: "It is known from the work of Klotz that amniotic filaments which have partly lost their attachment to the amnion remain at the connecting point with the fetal skin, and consisting of normal skin, sometimes reach a length of 2 cm. An amniotic filament (*faden*) that has prematurely lost its connection with the amnion either dies or perhaps in part is nourished by the fetus and takes on fetal characteristics—that is, is changed into tissue identical with that which arises from the same primary layers.

⁵ Monats. f. Geburtskunde, Band xxxii, 1868.

⁶ Archiv f. klin. Chir., 1888.

⁷ Ueber angeborene Unterlippenfisteln und Wärrchen. Dissertation, Berlin, 1891.

The papillæ and fistulæ of the lower lip are probably due to such amniotic rests acting as adherent filaments in the fetal furrow of the lower lip."

Stieda⁸ after reviewing the probable causes and the embryologic questions involved arrives at the following: (1) Fistulæ of the lower lip are not due to arrested fetal development. (2) Fistulæ of the lower lip arise from excessive growth through closure on both sides of the embryonal furrow of the lower lip—that is, through transformation of the lateral furrows into one canal. (3) The embryonal side furrows of the lower lip disappear usually during fetal life; in exceptional cases they persist throughout life. Stieda's case presented the typical picture in the lower lip, and also had harelip and cleft palate.



Case of congenital bilateral fistulæ of the lower lip.

Goldflam,⁹ in 1907, reported a case with no involvement of the upper lip, and agreed with Stieda's conclusions.

The only cases reported from America were published by de Nancrede¹⁰ in 1912.

De Nancrede found two cases in one family, the children presenting typical bilateral fistulæ of the lower lip, and offers the following explanation of the condition, by Dr. G. C. Huber, of the University of Michigan: "On either side the well-known median notch seen to persist some time during intra-uterine life after fusion of the two halves of the lower lip has been completed, it is not unusual to detect a slight secondary notching on each side. This becomes deeper, its deepest portion becoming gradually buried

⁸ Archiv f. klin. Chir., Band lxxix, No. 2.

⁹ Münch. med. Woch., January 8, 1907.

¹⁰ Annals of Surgery, September 1912, p. 400.

until a short tubular tract lined with mucosa is formed. Why this fixation of the deepest portions should occur, permitting the normal depth of the lower lip to develop, is of course conjectural."

The treatment of the fistulæ, when treatment is indicated, is by excision.

A CONTRIBUTION TO THE ETIOLOGY OF PERNICIOUS ANEMIA.¹

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IN 1860 Flint published his inferences regarding the atrophy of the stomach mucosa in cases of pernicious anemia. Ten years later Fenwick actually demonstrated the gastric lesion and worked out its pathology. Quinke, in 1876, was, however, the first, I believe, to consider the gastric changes as the causative factor of the anemia, while Martius, Lubarsch, and Koch considered the pathological findings in the stomach and intestines as secondary factors.

We appreciate now, however, that some hemolytic agent is present in the blood, and various theories have been advanced as to its origin. Hunter, in 1890, seems to have been the first to recognize this, and believed that some toxin was produced in the stomach in certain cases which was responsible for the hemolysis. Much pathological research was done to isolate this ptomain, and in 1898 Schauman, Faust, and Tallquist recovered a lipid substance from the segments of the bothriocephalus, which when administered to animals reproduced a blood picture resembling closely that of pernicious anemia. This they considered either a sodium or cholesterolin combination with oleic acid.

Ten years later, in 1909, Berger and Tsuchiya extracted a lipid substance from the gastric and intestinal mucosa of patients who had died from pernicious anemia, which showed hemolytic properties ten times stronger than extracts obtained in other conditions. They further reproduced, by animal injection of this extract, an anemia of the pernicious type.

Faber, who has probably made the most searching studies of the gastro-intestinal pathology in this disease, states that the changes noted in most intestines are postmortem, and will not be found present if the part is preserved immediately after death, but that the atrophy in the stomach is constant, and that in the stomach the etiologic factor must be sought for.

Herzberg, in a careful pathological study of 9 cases, concurs

¹ Read at the Fifteenth Annual Meeting of the American Gastro-enterological Association, and before the Brooklyn Society of Internal Medicine, November 22, 1912.

with Faber and believes that the gastric and blood phenomena in pernicious anemia arise from the same cause.

It is with the hope that some light may be thrown on this etiologic factor that the following observations are presented.

In the analysis of 433 cases of abdominal complaint presenting the symptoms of achlorhydria hæmorrhagica gastrica, most of which were observed at the Mayo clinic, there occurred during 1909, 1910, 1911, 34 cases of pernicious anemia. All cases of pernicious anemia presented the findings of an achlorhydria hæmorrhagica gastrica. Two cases of pernicious anemia examined one year before the blood dyscrasia evidenced itself showed lack of free hydrochloric acid and the presence of occult blood in the stomach extract. Many of them gave long histories of chronic digestive disturbances before there was any blood change, but no stomach analysis is recorded. Several developed marked paresthesia of the extremities when their blood showed as yet only a slight secondary anemia, with no evidence of a pernicious character.

Of the 433 cases of achlorhydria examined, 149 were operated on as they presented definite intra-abdominal disease. Gross pathological findings in these showed involvement of the appendix in 52 cases; the gall-bladder in 57 cases; the gall-bladder and pancreas in 21 cases, and the stomach in 19 cases. There were 19 cases in which the gall-bladder was diseased concomitantly with the appendix.

The anamnesis in 156 of the remaining cases developed the fact that the onset of gastric symptoms seemed to bear an immediate and direct relation to various diseases and conditions, among which the incidence of infectious diseases in 38 cases, circulatory disturbances in 12, postoperative development in 14, and derangement of the ductless glands in 20 instances, deserve mention.

Appreciating generally the extraordinary degree of gastric disturbance which irritation in distant organs can produce, it may be considered even more than a presumptive conclusion that reflex nervous phenomena are responsible primarily for the inhibition of the production of hydrochloric acid in these cases.

The bacterial flora present in cases of achlorhydria hæmorrhagica, achylia gastrica, and pernicious anemia are identical. Streptococci, colon, diplococci, lactic acid, staphylococci, proteus, and leptothrix are present in great numbers. Frequently all varieties may be seen in the same field so great is their profusion. In several instances the cells of the mucosa itself had taken on phagocytic properties. A chemical analysis can be foretold almost without exception from this picture of the bacterial flora under the microscope, and ample control of these observations by repeated examination of the flora existing in cases of hyperacidity, normal and hypoacidity, and in malignant and non-malignant stenoses seem to justify the following conclusions:

That in the stomachs of patients presenting the symptoms of lack of free hydrochloric acid there is present a very large number of bacteria. Varieties ordinarily pathogenic are almost universally found either alone or in combination; that their presence is dependent upon the lowered acidity of the gastric juice, that they are actively growing bacteria, evidenced by their profusion, morphological characteristics, and staining properties; that the streptococci are probably the most important factors, since they are found in large numbers in those cases where pus was noted.

My interest in this question of the bacterial content in the stomach in cases of achlorhydria and pernicious anemia was lately stimulated by an article by McCaskey, who was able to obtain from the blood cultures, streptococci in each of the cases of pernicious anemia examined by him, in two of which administration of an autogenous vaccine appeared to be instrumental in overcoming streptococcemia, and further remarks that all the cases in which fever was present in whom blood cultures were made, showed the presence of streptococci. This was significant when one appreciates that fever occurs in approximately 80 per cent. of cases of pernicious anemia. In further analyzing this phenomenon we find it continuing at times for weeks, or recurring periodically, but absent during the remissions which so frequently occur, and when, as Moffitt has noted, in certain cases of high temperature, profound exhaustion, nervous phenomena, and an enlarged spleen are noted they speak strongly in favor of an infective agency.

Fejes has demonstrated that anemia may be produced experimentally by bacterial hemolysins. Toxins produced by certain strains of streptococci have been shown to be distinctly hemolytic.

When one reflects upon the various means employed to treat pernicious anemia, the fact must seem apparent that possibly unconsciously they have all been working empirically to effect the same result, namely, the cleansing of the gastro-intestinal tract by the administration of medicines which we have lately learned to be germicidal in their action. Thus intestinal lavage, appendicostomy with colonic irrigation, administration by mouth of intestinal antiseptics, lavage of the stomach, thorough evacuation of the bowels, arsenic in its various forms, as Fowler's solution, and intravenous injections of salvarsan, autogenous vaccines, and finally hydrochloric acid.

I wish then to present for consideration these facts, namely:

1. Achlorhydria is merely a symptom denoting a marked degree of chronic gastritis.
2. It is usually evoked through extragastric irritative factors which are in many instances capable of correction.
3. There are, without exception, present in such stomachs great numbers of bacteria ordinarily considered pathogenic, among which streptococci are especially to be noted.

4. Practically all recorded cases of authenticated pernicious anemia present the symptom of achlorhydria, and in my own series of thirty-four cases the presence of occult blood in the stomach extract.

5. Thirty-four instances of pernicious anemia were noted in patients presenting the symptom of achlorhydria hæmorrhagica gastrica.

6. In a few of these cases the lack of hydrochloric acid and the presence of occult blood were known to be present at least one year before any blood changes were to be noted. In others the phenomena of paresthesia were evidenced some time previous to blood impairment, and many had suffered for years from chronic gastro-intestinal complaints.

7. Eighty per cent. of cases of pernicious anemia have increased temperature some time during the course of the disease.

8. Pure cultures of streptococci have been found by competent observers in the blood of patients with pernicious anemia who were running a fever.

9. Bacterial hemolysins are known to produce anemia resembling the pernicious type, as are other toxic substances, among which may be classed the lipid group.

10. Efforts directed to the control of bacterial growth in the body and particularly in the gastro-intestinal tract have caused complete remissions in this disease in some instances.

11. The phenomena of occurrence, remission, and re-occurrence of the blood picture characteristic of pernicious anemia may be explained by our present knowledge of the action of toxins from whatever source, impairing the formation of antibodies until a bacteremia is produced which may be clinically recognized.

12. The toxins we have present being eliminated by the profuse flora in the gastro-intestinal tract, the impairment of bodily resistance is accomplished through their absorption and the disturbance of digestion in cases of achlorhydria.

13. Finally, reactive and combative ability of patients suffering with achlorhydria varies in different patients, and on this ground alone might be explained the relatively rare occurrence of pernicious anemia, although the occurrence of achlorhydria is fairly common.

Thus the development of pernicious anemia would seem to be dependent upon a personal idiosyncrasy of certain individuals, in fact we must revert for the real etiologic factor of its inception to an embryonic tendency, the presence of which we are not as yet able to determine until it has been stimulated into an active destructive agent of the blood by the toxins absorbed from the profuse bacterial flora present in the stomach.

THE ROLE OF HYDROTHERAPY IN THE TREATMENT OF PELLAGRA.

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LIKE the task of firemen, who are compelled to fight the evident and rapid combustion of some huge and many-sided structure—not halting their efforts in order to discover its origin, nor abating their struggles to quench the flames, while others of their number are seeking the hidden source—so this problem of pellagra has been abruptly thrust upon the medical profession of the United States.

It has assumed menacing proportions with all the suddenness of a forest fire, and, while many earnest investigators have been delving at the etiologic questions involved, the actual therapy would not wait upon their discoveries or conclusions. Pellagra as a pathological entity has been placed before us, and of necessity we have had to administer some form of treatment, whether rational or otherwise.

The writer admits, with sorrow, that the etiology of pellagra is still in doubt. The zeists, or those who believe with the late Lombroso, that "In pellagra we are dealing with an intoxication produced by poisons developed in spoiled corn through the action of certain microorganisms in themselves harmless to man," are still in the majority. The antizeists, however, number among their ranks some doughty spirits, and we have the satisfaction of knowing that this important question will never be settled until it is settled correctly and beyond peradventure. In the meanwhile various procedures have been advocated, some apparently possessing merit; others most bizarre and fantastic.

It may be said that, with the exception of a few pessimistic individuals, who have found no distinctive pathologic lesions other than those coincident with senility, and therefore have consigned pellagra to the realm of incurable maladies, the larger number of those actually called upon to treat this disease have approached the difficult and obscure problems with a courageous feeling. They have evolved a fairly complete line of therapy, meeting with a large measure of success most of the indications, and their good results are not necessarily dimmed by the fact that some of their methods are empirical.

The medicinal, dietetic, hygienic, and even psychic treatment has been covered in recent literature, easily available to those interested. In hydrotherapy, though, we have an auxiliary whose helpful potentialities have not been sufficiently appreciated, and

whose aid may be invoked with confidence in some of the most distressing phases of pellagra.

No claim for originality as to methods is made, but in their special application to this protean disease the writer trusts that some new and worthy suggestions may be adduced.

Let it be briefly stated that in pellagra we have a fourfold syndrome—gastro-intestinal, dermic, nervous, and psychic—one or more units of which may predominate. Some of the typical cases may show at once all four units of the symptom-complex, but, as a general rule, one to three are manifested, while the others are partly or wholly in abeyance.

It is hard to imagine a more melancholy spectacle than a confirmed pellagrin, with his anorexia and indigestion and diarrhea; his parched and discolored hands, and perhaps face and feet; his burning tongue and extremities, coupled with shooting pains in different parts of the body; and often, overshadowing all, his changed mentality, varying in temperamental shade from indefinite blues to the blackness of melancholy and dementia.

Granted that all other possible therapeutic means are being assiduously employed, hydrotherapy may be advantageously used, first for gastro-intestinal symptoms. For the frequent and sometimes constant nausea the drinking of from two to six glasses of tepid water once or twice daily, so that by its emesis the stomach may be washed, will prove beneficial. Where it can be expertly performed, lavage once daily is better; but unless the medical attendant is an adept at introducing the stomach tube, lavage is best not attempted. In addition a cold water bag over the epigastrium placed there a half-hour before meals, and kept on fifteen to thirty minutes, plus drinking a half glass of iced water, exerts both a sedative and stomachic effect.

The frequent diarrhea may be greatly alleviated by hot colon irrigations, followed by cold sitz baths of five to ten minutes duration. This double procedure may be repeated two to four times daily when the patient is not too weak.

Another valuable method consists in the use of cold abdominal compresses, sometimes called "Neptune's girdle," in which the abdomen is encircled by a thick towel of liberal proportions, saturated with cold water. This may be removed and resaturated every one or two hours. Copious water-drinking is generally advisable, tending by its volume to keep the kidneys "flushed," and, by its solvent power, diluting and washing out many of the toxins. The diarrhea, being of central origin, and mainly compensatory in character, is rarely increased by an abundance of water in the body. Occasionally the writer has seen the bowels apparently regulated by this means after they failed to respond to astringent or dietetic endeavors.

For the occasional constipation, warm enemata, high if necessary, are always in order, and always efficacious.

To increase skin elimination there can be used the so-called "long bath" or various hot packs. A caution in regard to the use of the electric-light chamber is timely, for this is contraindicated in pellagra on account of the danger of kindling or increasing dermal symptoms. The skin of all pellagrins is peculiarly susceptible to the influence of any strong light, and the attending physician will avoid some troublesome complications by keeping this fact in mind.

For the dermal manifestations, expressed by erythema and sundry grades of dermatitis, hydrotherapy has but a limited field of usefulness. Apart from keeping clean the surface of the body, water has no specific effect; indeed, where the skin symptoms are markedly eczematous it is well sometimes to omit bathing the crusted surfaces for a brief season, using oily applications instead. In the occasional troublesome itching of the skin a cool or cold saline bath is often grateful. This may be made by the addition of chloride of sodium, seven pounds; chloride of magnesium, one pound; sulphate of magnesium, half pound; water, thirty gallons.

In many of the neuroses we derive most comforting results from hydrotherapy. The burning hands and feet may be greatly soothed by either ice-cold compresses applied at frequent intervals, or baths in hot mustard water. In addition may be employed hot leg-and-arm-packs, and revulsive compresses to the spine. In the use of the last named the hot compresses should stay on from three to five minutes, while thirty seconds will be sufficient for the cold. Three treatments daily, of thirty minutes' duration, are sufficient, and the relief obtained is often remarkable. These neuroses, being the painful expressions of lesions in the nerve centres, are most stubborn, sometimes remaining in evidence long after all other traces of pellagra have disappeared; and these special baths, packs, and revulsive compresses have proved helpful in a number of cases under the observation of the writer, where analgesics and anodynes had failed to afford any lasting cessation.

It is perhaps in those pellagrins where the psychic manifestations predominate that hydrotherapy holds the widest and most useful scope. For the mental disquietude with transient exhilaration, associated with insomnia, the neutral full bath at 94° to 96° , lasting from one to two hours, morning and evening, exerts a soothing effect. This may be augmented by warm compresses to the back of the neck, kept on about fifteen minutes, and applied three times daily. Should the patient seem somewhat autotoxic a free perspiration can well be induced at the end of these neutral baths by the use of hot packs, followed by suitable and brief cold applications.

He should also drink water freely. In this connection a daily

hot enema is often comforting even if not specially indicated by any abnormal bowel condition.

For mental depression and melancholia the cold percussion spinal douche bath exerts a decidedly good effect. If the patient is robust physically this douche bath may begin as low as 45° , but 65° to 70° is usually better. Should this not be agreeable, spinal sponging, alternating with hot and cold water, affords a passable substitute. Pellagra, being in the main an afebrile disease, cold packs are seldom indicated, though in some "typhoid" cases, with muttering delirium, they hold a doubtful place.

For the anemia and debility so often following in the wake of acute pellagra, cold measures, discreetly applied, yield not only a tonic effect but also an appreciable effect on the red blood count. This was proved by Prof. Winternitz as far back as 1893.

Practically all of these hydropathic measures, with the possible exception of the alternating douche, can be carried out at the home, though naturally a well-equipped institution, with trained attendants, can apply them with greater ease and precision.

The writer feels constrained to acknowledge valuable suggestions from Mr. W. W. Blackman, of Atlanta, whose wide experience in hydrotherapy, and painstaking efforts have demonstrated the utility of hydrotherapy in many instances.

Until a specific is found for this dread disease it is our duty to afford these forlorn sufferers every intelligent means of relief, and, from observation of over seventy-five pellagrins, with whom some form of hydrotherapy was employed, and in whom some measure of relief was noted in every instance, the writer presents it as worthy the thoughtful consideration of those who are burdened with the weight of this difficult problem.

THE ANALOGIES OF PELLAGRA AND THE MOSQUITO.¹

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WITH the publication of Sambon's *Progress Report*, in 1910, the investigation of pellagra really began. Before that time men studied a cereal, and thought they were studying a disease. Sambon's name will be associated with two great propositions concerning the nature and cause of pellagra: (1) The hypothesis that it is

¹ Read before the Second Triennial Congress on Pellagra, Columbia, South Carolina.

an infectious disease, and (2) the hypothesis that it is an insect-borne disease.

To many students these hypotheses stand as facts, because supported by much evidence and therefore believed; to others they are only hypotheses, and therefore only theories, because unproved. The third idea advanced by Sambon, namely, that the *Simulium* fly is the specific insect carrier, is open to far larger doubt than his first two propositions; and reasoning by analogy, and by the analogies of etiology, and by many notable comparisons, this fly is not nearly so apt to be the insect agent as is the mosquito.

The following objections hold against the *Simulium* as the disease carrier: So far as is known, the bite of the *Simulium* is poisonous rather than infectious; bearing toxins rather than parasites. The disease appears in America chiefly in those who are not field laborers, and who are little exposed to its bite. Pellagra occurs in sporadic cases in cities, among women who stay at home, and in asylums within doors, where the *Simulium* neither comes nor bites. It does not present the regularity of seasonal incidence, adults living through the winter, the repeated broods during spring, summer, and autumn, in enormous numbers as does the mosquito. It does not move in swarms far from its stream home, and, therefore, does not explain those cases arising at a distance from any running stream. It is more numerous in cold countries and on the coast of all continents, while pellagra avoids cold climates and seeks the interior rather than the coast.

The insect which carries the pellagrous parasite must account for and explain certain ecological and geographical facts of the disease, such as: Its seasonal relations, its periodicity, its recurrences, and its chronicity; its endemic relations, its occurrence chiefly in rural environments, its absence from cities except in sporadic cases; its peculiar geographical distribution over the world, in Africa along the Nile, in southern Europe, southern North America, and the West Indies; its predominance among females and in those who work around the house, as in women who wash clothes near the home; its attack on all ages and both sexes, infants, adults, and octogenarians; the spread of the disease in new areas, its epidemics, and their variations in severity; the severity of the disease in its first sweep of a new area, as in Roumania and America; and the increasing immunity to the disease in Spain and Italy, where it has raged for two centuries; its association with mosquito-borne diseases; its association with streams, swamps, foothills, valleys, lowlands, and standing water in damp areas.

The following analogies of etiology and comparisons with mosquito-borne diseases show a relationship to a common insect host, the mosquito.

Pellagrins are insane, become inmates of asylums, and insane inmates conversely become pellagrous, as in the Alabama epidemic

reported by Searcy, the Illinois asylum cases reported by Zellar, the Jamacia cases reported by Williams. The two sexes are more equally affected in those who develop the disease within the asylums, and within doors both sexes are equally exposed to the infecting agent. The insect probably lives and bites in houses.

In Italy, Roumania, and America pellagra predominates in females and in those individuals of both sexes that remain in and around the home during the day. They are more exposed than those away from home working in the fields or woods.

The mosquito accounts for the fact that a woman in the family may become pellagrous, and other women in the same house develop the disease. They are together day and night equally exposed to the infecting agents. On account of this spread of the disease in one family, under one roof, chiefly among women and children, it has in certain endemic areas been considered contagious, as was yellow fever before the *Stegomyia fasciata* was discovered to be the agent in its distribution.

For pellagra to appear in the United States, either the parasite or both parasite and insect host must have been lately introduced. For it to spread the parasite must be naturally fitted to the climate, seasons, and to insect and human hosts; the insect host must be adapted to climate, seasons, habitat, and environment. For such adaption to exist on the part of the insect it must have been in America many centuries and in enormous numbers. The parasite of pellagra has, therefore, probably been recently introduced, and its specific insect host is a natural, long time inhabitant, present in enormous numbers, as is the mosquito. For instance, *Stegomyia fasciata* was found in Milledgeville, Georgia, in September, 1912, in a soft-drink stand, but the yellow fever agent was lacking, and there was no yellow fever in the city.

Like malaria and filariasis, pellagra is chiefly rural. Rome escapes malaria, and yet in the marshes without the city the disease rages. Bucharest, Milan, and Atlanta escape pellagra, but in the regions round about the disease persists. Even in large cities sporadic cases of malaria and pellagra develop, they usually occur on the outskirts, where the drainage is poor and filth and sewerage abound.

Pellagra has an unquestioned relation to streams, swamp areas, standing water, and places that breed the mosquito, as have malaria and yellow fever. This is true in Egypt along the Nile, in Greece, Roumania, Italy, Spain, and America.

Hills tend to escape in areas visited by pellagra, malaria, yellow fever, and filariasis.

In areas both malarial and pellagrous, rains and floods that increase malaria, also increase pellagra. With the proper drainage of such an area, both diseases decrease and later disappear, as illustrated by the Landes in southern France.

Mosquito-borne diseases have a seasonal incidence. Yellow fever in spring, summer, and autumn; malaria in spring, summer, and autumn; pellagra in spring, summer, and autumn. Yellow fever depends in its endemic areas upon the time of the appearance of the *Stegomyia*; malaria upon the *Anopheles*; pellagra upon its specific mosquito host. The first attack of pellagra may develop any time from early spring to fall, for the reason that several broods of the mosquito host appear during this period.

Malaria, yellow fever, filariasis, and pellagra tend to appear and become epidemic with spring and early summer. Within the bounds of latitude the outbreak of these diseases is later in the spring and summer as one goes farther North, and earlier as one goes farther South. The annual pellagrous attack tends to be earlier the second summer, and the earlier the spring season the sooner the attack; this is also true of malaria.

Pellagra appears and persists in cotton-mill communities in the South, and is absent from cotton-mill and factory communities in the Eastern States. There is probably an infected mosquito in the South which is absent from the East. The usual factory reservoir, the puddles of water, the surface closets, the washtubs in every back yard, the rain-water barrels, the mosquito-breeding areas, the women at home, are all consistent with the mosquito as a reasonable hypothesis.

Malaria, yellow fever, filariasis, and pellagra all tend to cease spreading, the cases improve, and the disease dies away with the coming frost, cold, and winter. All these diseases avoid the winter because of the influence of the cold season upon both parasite and insect.

Pellagra, like malaria, yellow fever, filariasis, and dengue fever, has its epidemics, its years of severity and mildness, its ebb and its flow of prevalence and of intensity.

Pellagra, malaria, yellow fever, and filariasis are all endemic in restricted areas for a century, and epidemic at different times. These endemic areas are mosquito breeding-areas, and in times of epidemic mosquitoes are present in great numbers.

Pellagra and malaria have latent periods and periods of activity, due to the change in the seasons, the fixed life-period of the parasite, and its alternating periods of activity and rest; and to changes in climate, altitude, and vitality. Spring may usher in an attack of malaria or of pellagra. A surgical operation or a confinement may float a latent pellagra or a latent malaria.

Pellagra, malaria, yellow fever, and filariasis are non-contagious and non-inheritable.

The incubation period in malaria is ten days to three weeks; in yellow fever thirty-six hours to fourteen days; in pellagra probably two to three weeks, certainly less than four weeks. Sambon recently found pellagra in an infant one month old. This fact signifies kinship of insect carriers.

The parasites that cause malaria, yellow fever, and filariasis are more restricted in their endemic areas and in their geographical distribution than their insect hosts. *Anopheles* has a wider distribution than the *Plasmodium malariae*; *Culex fatigans* than the *Filaria bancrofti*, and *Stegomyia fasciata* than the yellow fever agent. The same relational distribution of parasite and mosquito probably applies to pellagra.

Pellagra is absent from Ireland, where *Simulium* flies occur in abundance, but mosquitoes are relatively scarce. Malaria, yellow fever, filariasis, and dengue fever are also absent from Ireland. Furthermore, the poorest Irish peasants, whose poverty is famed and world-wide, eat Irish potatoes and "yellow meal," the latter being imported as shelled corn from America, Africa, and Russia through the Baltic Sea, and yet there is no pellagra in Ireland.

Scotland,² practically all of England, and Australia are free from pellagra, malaria, filariasis, and yellow fever. Canada is likewise free from all these diseases, except a small area on the shore of Lake Ontario, where a few malarial cases occur. Except for Illinois, where five hundred cases of pellagra have occurred, and a few sporadic cases in the northern and western United States, pellagra, malaria, and yellow fever all tend to remain in the southern United States and farther southward. A further significant fact is that the Illinois cases are chiefly asylum cases.

Practically all pellagrous areas are also malarial areas, except in the small island of Barbadoes in the West Indies, where pellagra, yellow fever, and filariasis occur, but no malaria. On the nearby island of Jamaica, however, all four diseases exist, pellagra, malaria, yellow fever, and filariasis. Pellagra is to Italy and Roumania what yellow fever is to the West Indies, and what malaria is to Greece and to the foothills of the Himalayas in India.

Pellagra extends from 8° to 45° north latitude. Forty degrees north latitude cuts the pellagrous area of Europe into northern and southern halves, and 45° mark its northern limit; 30° north latitude cuts the pellagrous area of Africa; and the same parallel cuts the North American area, with 8° in Panama as the southern and 45° in New York as the northern limit even in sporadic cases. The distribution of pellagra in three continents is marked by an average latitude of 30° to 45°, and 90 per cent. of the pellagra cases in the world occur in this belt of 15°, or a distance of 1000 miles from north to south. In this belt occur also malaria, yellow fever, filariasis, dengue fever—all the mosquito-borne diseases. Furthermore, while *Anopheles* occurs in this area, the northern distribution of pellagra generally marks the northern limit of *Stegomyia fasciata*, and the household mosquito, *Culex fatigans*. In pellagrous territory on three continents are these three mos-

² Sambon thinks pellagra exists in Scotland.

quitoes. If the *Simulium* were the insect carrier, we should expect pellagra in northern as well as southern Europe, in Ireland as well as in Italy, in Minnesota and Canada as well as in Georgia and Panama.

Returning now to the ecological and geographical facts of the disease, the mosquito accounts for its seasonal relations, periodicity, and recurrences; its endemic relations, rural habitat, and sporadic appearances in cities; its peculiar geographical situation in Africa, Europe, and America; its predominance among females and those who stay much at home; its attack on all ages and both sexes; the spread of the disease in new areas; its first sweep of severity in such areas, and later its gradual decrease and the relative immunity of the inhabitants; its presence along streams and in mosquito-breeding areas.

Whether a single species of the *Culicidæ* harbors the pellagrous parasite, as in yellow fever, or more than one, as in malaria, and what this particular species may be, is a question for the future. It will probably prove to be a rural breeding, house-living, day-biting mosquito. To us and perhaps to those who shall come after us the problem remains—the investigations, the experiments, and the proof.

AN INTENSIVE STUDY OF THE EPIDEMIOLOGY OF PELLAGRA. REPORT OF PROGRESS.¹⁴

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(Concluded from page 66, July, 1913.)

PART II.

XII. RELATIVE PREVALENCE, SEVERITY, AND MORTALITY RATES IN RECENT YEARS. Pellagra is not a reportable disease in the State of South Carolina, nor do the State laws require notification of deaths from pellagra to the health authorities.

¹⁴ From the Thompson-McFadden Pellagra Commission, New York Post-Graduate Medical School and Hospital.

The data to be analyzed were obtained from a number of sources. The 282 cases studied in detail by the Commission afforded one source. In the City of Spartanburg, official records are on file covering deaths from all causes within the city, and thus it was possible to secure accurate mortality statistics for the city. There are some five or six undertaking establishments in the county, as a whole, and the two establishments in the city of Spartanburg sell very nearly all the coffins used throughout the county. These two establishments keep on file the names, causes of death, and other information concerning the deceased for whom coffins are furnished, and they very courteously permitted us to make abstracts from their records. From these records we obtained information of importance. From the members of the medical profession throughout the county we secured much valuable information relating to prevalence and mortality rates for 1912 and previous years. From pellagrins themselves and from others we were able occasionally to obtain information concerning individual cases. Dr. Babcock, of South Carolina, kindly furnished us with information covering the cases admitted to the State Hospital for the Insane from Spartanburg County.

Although we availed ourselves of all these sources of information, we wish to emphasize the fact that this study is still far from complete. We hope, however, to make it more comprehensive and complete during the course of our studies in the same county in the summer of 1913.

The opinion was expressed by many physicians in Spartanburg County, that pellagra was not so prevalent in 1912, as was the case in 1911. We might say, further, that a like impression prevailed in many other parts of South Carolina and in other Southern States.

The statistical data at hand for Spartanburg County are subject to analysis in several ways:

1. From the information available we have determined as nearly as possible the actual number of cases of the disease existing in the county each year, without consideration of the year in which the disease was contracted and without reference to recurrences.

In 1912	there were 376 cases (minimum).
In 1911	there were 285 cases (minimum).
In 1910	there were 115 cases (minimum).
In 1894 to 1910	there were 114 cases (minimum).

It is quite evident that pellagra was not recognized as such, to any extent, until the year 1909.

We have endeavored to secure from the practising physicians in the county accounts of the first and other early cases occurring in their practices. As yet this information is incomplete, but it establishes the fact that the disease has existed in the county

sporadically for a number of years. Dr. Fike of Spartanburg, has the record of a patient dying of pellagra in 1894, although not at the time recognized as such. The patient was an adult female, and three other members of her family are said to have died of the disease. One of the first cases which developed in the city of Spartanburg was that of a young woman in a well-to-do family. She contracted the disease and died of it in 1902. Dr. Jefferies, of Spartanburg, has the record of a patient who died of pellagra, in November, 1903, but the disease was unrecognized as such until years afterward.

While there is no doubt that pellagra has existed in this section for a number of years, information obtained from the medical profession throughout the county indicates very clearly that the cases must have been more or less sporadic until within recent years. The general impression is held that sporadic cases occurred until about 1909, at which time there was a marked increase in the number of cases; that during 1910 and 1911 the disease became more prevalent; while in 1912 there was a slight decrease in incidence. The perceptible increase of cases in 1909 may be accounted for in part by the fact that the disease was not until then generally recognized as pellagra. We have consulted with many medical men in Spartanburg County and in other parts of South Carolina, and in other States, and it is our belief that the large number of cases recognized in 1910 and 1911, as compared with the number recognized previous to that time, cannot alone be explained on a basis of general failure to recognize the disease in earlier years. Non-recognition unquestionably explains some of the increase, but we are thoroughly convinced that there has been an actual and quite perceptible increase in the number of cases within the past three or four years.

2. A second analysis of our data shows that the minimum number of cases of pellagra in Spartanburg County from 1894 to October, 1912, was 495. This is obviously a conservative estimate, as prior to 1911 our data are made up largely of cases in which the disease terminated in death.

3. We have endeavored to determine the actual number of new cases of the disease occurring each year. It is possible to determine this with a reasonable degree of accuracy for 1912 and with a fair degree of accuracy for 1911, but prior to that time the incidence rates (annual) are altogether a matter of conjecture. We have seen that there were at least 376 cases of pellagra in Spartanburg County in 1912. Of the cases seen during our study in 1912 (282), 97 contracted pellagra in 1912, and of 94 others not included in our series we have knowledge of the fact that 16 contracted the disease in 1912. The minimum total of new cases for 1912 is thus 113. In 1911 the total number of cases in the county was 285. Among the cases included in our series (282), 100 contracted pellagra in 1911, and we have record of 20 other cases contracting it in 1911,

making a total of 120. Of the remaining 165 cases existing in the county in 1911 the information at hand is more or less indefinite, but unquestionably some of this number contracted the disease in 1911.

Prior to 1911 definite statistics are too meagre to warrant analysis. Our statistics suggest that pellagra, so far as new cases are concerned, was somewhat more prevalent in 1911 than in 1912.

The annual case death-rate among pellagrins was as follows:

Year.	No. of deaths.		No. of cases.	Per cent. of deaths.
Unknown	8	}	25	114
1894	1			
1898	1			
1899	1			
1901	2			
1902	2			
1903	1			
1904	1			
1908	2			
1909	14			
1910	32		115	28
1911	54		285	19
1912	47		376	12

It should be understood that these mortality statistics are of pellagrins who have died from all causes, not deaths from pellagra alone. In a number of these cases the pellagrous symptoms were of but little moment, the actual causes of death being other factors, among which may be mentioned tuberculosis and senility. The morbidity and mortality statistics for 1910 and the years preceding are not sufficiently complete to warrant any deductions. Those for 1911, showing 19 per cent. deaths, and for 1912, showing 12.5 per cent. deaths, represent more nearly the relationship between the morbidity and mortality rates as they exist at present.

Death during the initial attack is not uncommon. In the series of 282 cases studied by this Commission, 97 contracted the disease in 1912, and 5 of these cases died during the initial attack.

SUMMARY. The following general statements concerning relative prevalence and mortality seem to be warranted:

Sporadic cases have been observed in Spartanburg County since 1894. During the past three or four years there has been an alarming increase in the number of cases. The number of new cases developing in 1911 was somewhat greater than in 1912, although the difference was but slight. When the disease first appeared in Spartanburg County the symptoms were frequently severe and the death-rate appears to have been high. The number of cases in the county is increasing while the death-rate appears to be decreasing.

XIII. CLINICAL OBSERVATIONS ON PELLAGRA. A. *Chronicity and Periodicity, with a Study of the Influence of Climatic Conditions.*

1. *Chronicity.* We have observed no differences in the symptomatology, and more particularly in the chronicity, of the disease as

it exists in this country and in Italy, except the fact that the mortality rates in this country two or three years ago were apparently much higher than those obtaining in Italy at the same time. A few of the cases in the present series died during the initial attack in 1912, while others presented a wide gradation of symptoms ranging from those involving the cutaneous, gastrointestinal, and nervous systems to those in which the cutaneous system alone was involved.

ORIGINAL ATTACK AND ANNUAL RECURRENCES.

Early history indefinite; recurrence, 1912	1
1904.	
First attack, 1904; recurrences, 1905, 1906, 1907, 1908, 1909, 1910, 1911, 1912	1
1905.	
Indefinite history, 1905 to 1911 inclusive; recurrence 1912	1
First attack, 1905; recurrences, 1906, 1907, 1908, 1909, 1910, 1911, 1912	1
1906.	
First attack, 1906; recurrences, 1907, 1908, 1909, 1910, 1911, 1912	1
1907.	
First attack, 1907; recurrences, 1908, 1909, 1910, 1911, 1912	1
First attack, 1907; no clear history, 1908, 1909, 1910; recurrences, 1911, 1912	1
1908.	
First attack, 1908; recurrences, 1909, 1910, 1911, 1912	2
First attack, 1908; recurrences, 1909, 1910; no recurrence, 1911; recurrence, 1912	1
First attack, 1908; no recurrences, 1909, 1910; recurrences, 1911, 1912	1
First attack, 1908; recurrence, 1909; no recurrence, 1910, 1911, 1912	1
1909.	
First attack, 1909; recurrences, 1910, 1911, 1912	11
First attack, 1909; indefinite history, 1910, 1911; recurrence, 1912	1
Indefinite history, 1909, 1910, 1911; recurrence, 1912	1
First attack, 1909; no recurrence, 1910; recurrence, 1911; no recurrence, 1912	1
First attack, 1909; no recurrences, 1910, 1911, 1912	1
First attack, 1909; recurrences, 1910, 1911; no recurrence, 1912	1
First attack, 1909; no recurrences, 1910, 1911; recurrence, 1912	1
First attack, 1909; recurrence, 1910; no recurrence, 1911; recurrence, 1912	1
1910.	
First attack, 1910; recurrences, 1911, 1912	30
First attack, 1910; no recurrence, 1911; recurrence, 1912	3
First attack, 1910; recurrence, 1911; no recurrence, 1912	12
Indefinite history, 1910; recurrences, 1911, 1912	1
First attack, 1910; no recurrence, 1912	3
First attack, 1910; no history, 1911, 1912	1
1911.	
First attack, 1911; recurrence, 1912	69
First attack, 1911; no recurrence, 1912	29
Indefinite history, 1911; no recurrence, 1912	1
Indefinite history, 1911; recurrence, 1912	1
1912.	
First attack, 1912	97
Total	277

It will be noted that in some of these cases the disease was contracted originally in 1904; in others, in 1905 and every year thereafter to 1912, inclusive. Occasionally the history of previous attacks was indefinite, and such cases are so classified.

In this series there are 55 cases of pellagra recognized from one to five years ago by the attending physicians in which the annual recurrence has failed to appear in one or more seasons. In some of these cases the disease has reappeared after an intermission of one or two years, while in other instances symptoms have been present for one or more seasons, and have never since recurred. The following cases illustrate this point:

First attack, 1908; recurrence, 1909; no recurrences, 1910, 1911, 1912	1
First attack, 1909; no recurrences, 1910, 1911, 1912	1
First attack, 1910; no recurrences, 1911, 1912	3

In addition to these five cases we have records of a few other cases in Spartanburg County, not included in this series, in which patients have been without symptoms for a period of two, three, or more years and appear to be cases of recovery from the disease.

Our individual case histories show that a number of adult females have borne children since contracting pellagra, but in only 22 cases is the relationship of the pregnancies to the development of symptoms sufficiently definite to warrant analysis. In 16 of these cases (75 per cent.) there were no symptoms of pellagra during pregnancy. These observations cover only a small number of cases, and this subject will be investigated more in detail in this series and in additional ones during the summer of 1913. Pregnancy seems to show a tendency to inhibit the development of pellagrous symptoms.

2. *Periodicity.* A study of the literature of pellagra gives one the impression that there is a definite seasonal periodicity. We are led to believe that the disease appears in the spring; that there is a relative decrease in the number of cases in midsummer; that a fall recrudescence occurs, and that there is a tendency for symptoms to reappear at the same time each year.

Samson cites the spring and fall periodicity as a strong argument in favor of his hypothesis that the disease is of protozoal origin and transmitted by a blood-sucking insect, a species of *Simulium*.

We have undertaken some studies bearing on this phase of the subject. It is evident that these observations, except for the year 1912, must be based on the statements of patients suffering with pellagra. We have endeavored to control such statements and to add to their reliability by information obtained from other members of the household, and more particularly by that obtained from the attending physician. The cases will first be considered by month of onset of symptoms. Chart 9 represents graphically the month of onset of symptoms arranged by years. It is understood, of course, that this chart represents not only the month of original

onset in each case, but includes also the recurrences in each case year by year.

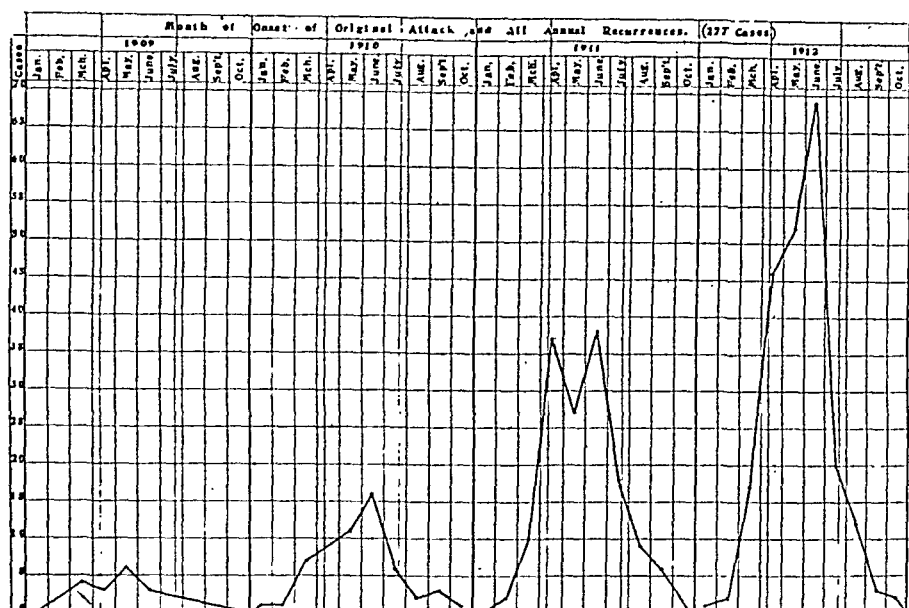


CHART 9.—Month of onset of original attack and all annual recurrences (277 cases).

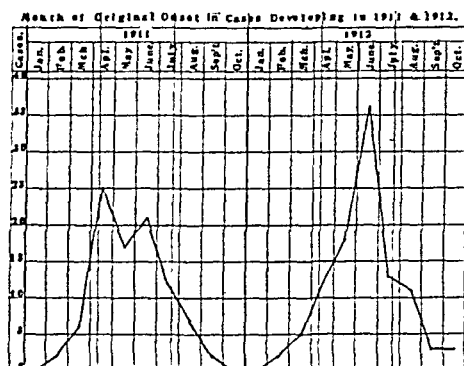


CHART 10.—Month of original onset in cases developing in 1911 and 1912.

In Chart 10 we have analyzed further the 1911 and 1912 cases from the standpoint of original onset of symptoms when the disease was contracted. It is evident from these charts that cases begin to show symptoms in the early spring, that there is a gradual increase in the number showing symptoms until the month of June, when the incidence curve reaches its highest point, and that after the month of June the incidence-rate falls quite rapidly. It is also evident that there are no spring and fall recrudescences of pellagra in Spartanburg County. On the contrary, cases begin to show symptoms in the spring, increase in number until mid-summer, and then rapidly decrease.

We have analyzed the recurrent attacks with a view of determining whether or not there was any marked tendency in each individual case for active symptoms to appear during the same month year after year, with the following results:

INTERVAL BETWEEN ONSET OF SUCCESSIVE ATTACKS.

	11½ to 12½ months.	11 to 11½ months or 12½ to 13 months.	Less than 11 or more than 13 months.
Cases contracting pellagra in 1909	4	2	5
Cases contracting pellagra in 1910	12	17	10
Cases contracting pellagra in 1911	21	20	24
	—	—	—
	37	39	39

We have analyzed still further the uniformity of recurrences, first by ascertaining the date of appearance of symptoms in individuals who contracted the disease in 1910 and comparing these dates with date of recurrence of symptoms in the same individuals in 1911, and second, by tabulating the same facts for cases developing originally in 1910 and 1911 and recurring in 1912.

Among the cases showing symptoms originally in 1910 the recurrence in 1911 was a month or more earlier in 14 cases, during the corresponding month in 27 cases, and a month or more later in 17 cases. Among the cases contracting the disease in 1910 and 1911 the recurrence in 1912 was at least a month earlier as compared with the appearance of symptoms in 1911 in 36 cases, during the same month in 48 cases, and at least a month later in 33 cases.

It is evident from this analysis that there is no particularly marked tendency for the seasonal recurrences to reappear during the same month year after year.

3. *Influence of Climate.* Climatic conditions are said to influence the periodicity of the disease. If during the spring months the precipitation is high, temperature low, and number of rainy days excessive, there is said to be a delay in the appearance of acute symptoms, more particularly those involving the skin. One of us had occasion to observe this influence in the spring of 1910 while investigating conditions in northern Italy. In March and April of that year the weather conditions in the provinces of Milan and Bergamo were quite unsettled, precipitation was excessive, there were many rainy days, but little sunshine, the temperature was low and the atmosphere was damp and chilly. At this time there were but few cases showing active symptoms of pellagra. The delay in appearance of active symptoms was attributed to unsettled weather conditions. We were informed, further, that it had been observed for many years that unsettled weather conditions in the spring always delayed the appearance of active

symptoms of the disease. We have been able to compare this general impression as regards conditions in Italy with similar conditions in the South. Early in May, 1912, we investigated the prevalence of pellagra in different sections of South Carolina, in North Carolina, and in Georgia. The physicians consulted informed us that there was a delay in appearance of cases showing active symptoms, and that whereas in April, 1911, they had observed many such cases, in April, 1912, they had seen but few. We were informed that spring and settled weather conditions were present much earlier in 1911 than was the case in 1912. This general impression is confirmed by the fact that farmers in the states mentioned were able to get their crops under way quite early in 1911 while in 1912 they were delayed for from three to six weeks. In Spartanburg County it was possible to secure much more detailed information covering weather conditions. The general information given us is in agreement with that outlined above.

In order that these general impressions may be controlled, we have obtained from the United States Weather Bureau its reports on weather conditions in Spartanburg County, South Carolina. The available information from this source, which includes monthly precipitation, monthly mean temperature, and number of rainy days, is presented in Charts 11, 12, and 13.

It is evident from an analysis of the monthly precipitation curves for 1911 and 1912 that in 1912 during the months of January to June inclusive, except for the month of April, the monthly precipitation was greatly in excess of that for the like period in 1911.

Analysis of the monthly mean temperature curve for 1911 and 1912 shows that in 1912 for the months of January to June inclusive the temperature was, in general, appreciably lower than was the case for like months in 1911.

A study of Chart 13 (number of rainy days) shows that for the first six months in 1912, except for the months of March and April, the number of rainy days per month was in excess of the number for the like period in 1911. While there were more rainy days in March and April, 1911, than for the same months in 1912, the amount of precipitation for these two months in 1912 was in excess of that for 1911.

These charts, considered as a whole, indicate quite clearly that settled weather conditions with relatively high temperature and low precipitation existed in Spartanburg County at an earlier date in 1911 than was the case in 1912.

The relationship between climatic conditions existing in 1911 and 1912 and the appearance of acute symptoms of pellagra can be determined by referring to Charts 9 and 10. There was quite a definite tendency for symptoms to appear at an earlier date in 1911 than was the case in 1912. The incidence-rate in both charts was high for the month of April, 1911, while in 1912 the incidence-

rate for April was comparatively low, especially in respect to new cases, and the maximum rate was not attained until the month of June.

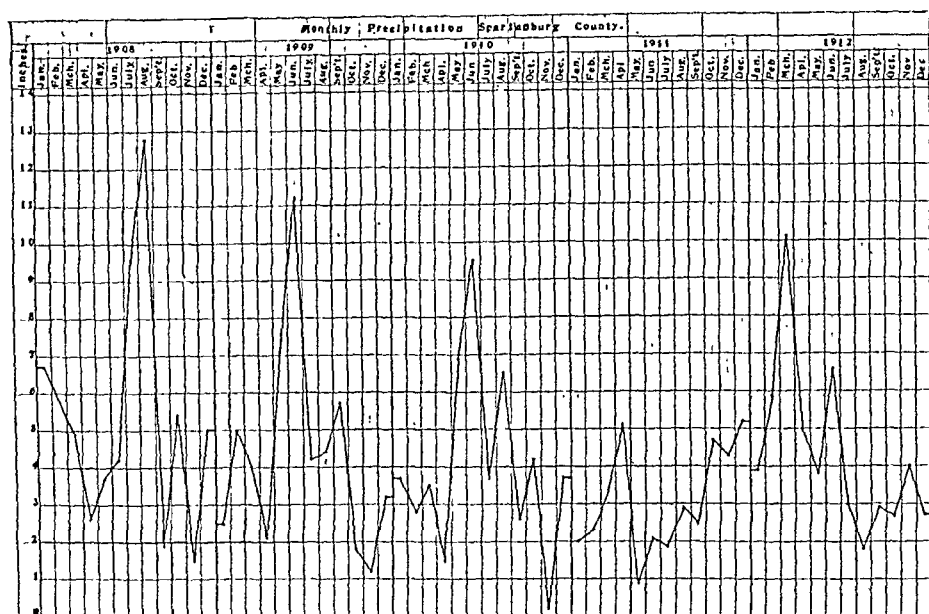


CHART 11.—Monthly precipitation, Spartanburg County.

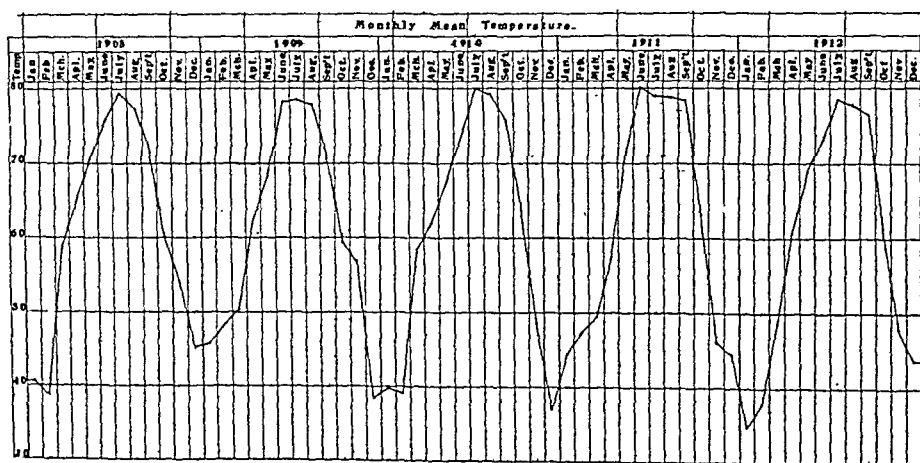


CHART 12.—Monthly mean temperature.

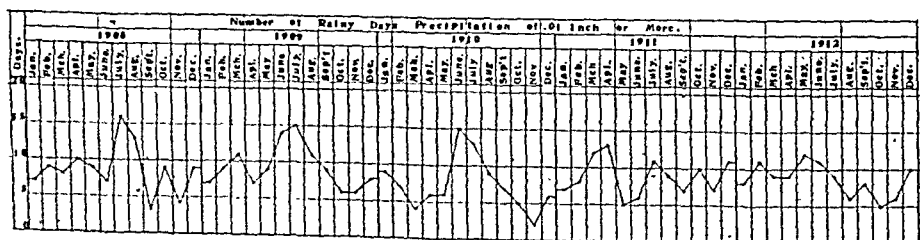


CHART 13.—Number of rainy days, precipitation 0.01 inch or more.

SUMMARY. 1. *Chronicity.* In a large proportion of the cases in this series the disease exhibited marked chronicity. In 20 per cent. the annual recurrences had failed to appear in one or more seasons. Pregnancy seems to show a tendency to inhibit the development of pellagrous symptoms. In 2 per cent. of the cases no symptoms had been present for from two to three years, and these appear to be cases of recovery from pellagra.

2. *Periodicity.* Cases begin to show symptoms in the early spring, increase in number until midsummer, and then rapidly decrease. There was no evidence whatever pointing to any spring and fall recrudescences, so frequently referred to in the literature of pellagra. There is no particularly marked tendency for the seasonal recurrences to appear during the same month, year after year, in the same individual.

3. *Influence of Climate.* Climatic conditions appear to influence the development of symptoms of the disease. If during the spring months precipitation is high, temperature low, and number of rainy days excessive, the appearance of acute symptoms, more particularly those involving the skin, is delayed.

B. *Symptomatology of 1912 Attacks.* A considerable amount of information has been collected in reference to symptomatology, but a discussion of this phase of the subject will not be undertaken until we have followed these cases through their 1913 recurrences.

The following general statements are warranted: While three or four years ago it was quite the usual thing to see patients showing a combination of severe skin lesions, severe stomatitis, intractable diarrhea or dysentery, mental derangement, and physical exhaustion, comparatively few patients exhibiting this symptomatology in a marked degree were observed in Spartanburg County during the summer of 1912. In many of the cases observed the symptoms were quite mild, and frequently they were confined almost entirely to the cutaneous system. This apparent indication of a decreasing virulence of the disease is strengthened by certain facts which appear in the study of mortality rates of pellagra in Spartanburg County for 1912 and earlier years.

XIV. CLINICAL OBSERVATIONS UPON ECONOMIC STATUS AND PREVIOUS HEALTH OF PELLAGRINS. It is believed by many who are brought into contact with pellagra that predisposition plays an important part in its development and that the disease most frequently affects the poorer classes, who live under unfavorable hygienic conditions and who subsist on a diet of low nutritive value and of limited variety. Some detailed studies were undertaken covering these points. The general hygienic conditions and dietary will be discussed elsewhere, and this section will be confined to a consideration of financial circumstances and health conditions as possible predisposing factors.

A. *Economic or Financial Circumstances.* In recording the data relating to the economic conditions under which the patients lived, the following classification was adopted: squalor, poverty, necessities, comfort, affluence. These terms are somewhat arbitrary and necessitate some brief explanation.

Squalor. Cases so classified are confined to those living in wooden huts in poor repair and without out-houses. Their diet was extremely poor and without variety, living rooms squalid, clothing filthy and in rags.

Poverty. Cases of this class lived in cabins usually without out-houses, rather isolated, ordinarily on large plantations. Food consisted largely of bacon, molasses, corn-bread, and biscuit. Negroes of the poorer tenant class form this group very largely.

Necessities. This class included those instances in which the family had a fairly regular cash income sufficient to provide for actual needs. It is made up largely of mill operatives and their families. They live in cottages, with some land about them, but rather closely aggregated to form mill-villages.

Comfort. Cases classified in this group are made up largely of farmers who own their own plantations and stock, have a good diet, and are in comfortable financial circumstances.

Affluence. In this group are included patients who live under the best of hygienic and financial conditions. Their houses are well-constructed, usually screened, and their diet is well balanced.

The cases so classified number 277 and are divided as follows:

Squalor	2
Poverty	28
Necessities	200
Comfort	41
Affluence	6

It will be seen that in 83 per cent. of the cases (squalor, poverty, necessities) the economical conditions were poor; that in 15 per cent. (comfort) the economical conditions were within the average, and in 2 per cent. (affluence) the financial circumstances were well above the average.

In connection with the "affluence" group, it may be said that the members of the Commission have personal knowledge of a number of other instances in which pellagra has developed in persons living under the best of hygienic and economic conditions.

Grouping the cases under two general subdivisions, we find that in 83 per cent. of the cases the economic conditions are poor, while in 17 per cent. they are good.

B. *Diseases of Childhood and General Health in Childhood.* *Diseases of Childhood.* In considering the diseases of childhood the cases were divided in two groups: (1) those giving a history of one or more of the following diseases: measles, mumps, chickenpox,

and whooping cough; (2) those giving a negative history for the diseases of childhood. The data covered 270 cases.

DISEASES OF CHILDHOOD.

Cases giving a history of one or more of the following diseases of childhood: measles, mumps, whooping cough, and chickenpox	252
No history of diseases of childhood	18
Total	270

As permanent injury to the heart and kidneys not infrequently follows attacks of scarlet fever, this disease was considered separately. In 20 cases a history of scarlet fever was elicited.

General Health in Childhood. The classification adopted in the consideration of general health in childhood was the following: Good, fair, and poor. Inquiries covering this point were made in 270 cases. Of this number, 232 (86 per cent.) gave a history of good health during childhood; in 28 cases it was fair, and in 10 cases it was poor.

C. Diseases of Adult Life and General Health during Adult Life. *Diseases of Adult Life.* The total number of cases considered is 198. The diseases peculiar to female adult life will be considered in a separate table. The following summary shows the prevailing diseases in some detail:

	No. of cases.
Gastric disturbance	14
Dysentery, acute or chronic	28
Typhoid fever	46
Tuberculosis	7
Other diseases, unclassified	36
No history of ill health	67
Total	198

An analysis of diseases of adult life shows that 34 per cent. (67) of the total number of cases gave no history of ill-health. In 25 per cent. of the cases, those giving history of gastric disturbances, dysentery, and tuberculosis, a chronic disease was present.

General Health in Adult Life. In considering this point the classification adopted was that of good health, fair health, and poor health.

GENERAL HEALTH DURING ADULT LIFE.

Good	134
Fair	66
Poor	18
Total	218

An analysis of the data concerning general health conditions during adult life shows a history of good health in 62 per cent., fair health in 30 per cent., and poor health in 8 per cent.

D. Obstetrical and Gynecological History.

SOCIAL STATUS.

Married	150
Widowed	9
Single	25
	<hr/>
	184

OBSTETRICAL HISTORY.

Married females who have borne children	136
Unmarried females who have borne children	2
Married females who have not borne children	23
Unmarried females who have not borne children	23
	<hr/>
	184

Number of females who have borne 1 child	28
Number of females who have borne 2 children	20
Number of females who have borne 3 children	21
Number of females who have borne 4 children	25
Number of females who have borne 5 children	16
Number of females who have borne 6 children	8
Number of females who have borne 7 children	10
Number of females who have borne 8 children	4
Number of females who have borne 9 children	3
Number of females who have borne 10 children	1
Number of females who have borne 11 children	2
	<hr/>
	138

Average number of children borne = 3.8.

MENSTRUATION DURING PERIOD OF ACUTE PELLAGROUS SYMPTOMS.

Normal	95
Irregular	53
Excessive	6
Suppressed	10
Menopause	11
No information	9
	<hr/>
	184

DISEASES OF WOMEN.

Number of females giving more or less definite history of ovarian, uterine, or other pelvic disease	49
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From this summary it will be noted that among the females who had attained the age of puberty, 86 per cent. of the cases occurred in married women, and that 86 per cent. of these married women had borne children. The greatest number of children borne by an individual is 11. The average number borne is 3.8. We have collected some statistical information in reference to the average size of families in mill-villages in Spartanburg County, from the standpoint of children borne by each woman, and it is not significantly different from the average number shown among pellagrous women.

The amount of time at our disposal and the relative importance of the subject did not warrant examinations of sufficient thoroughness to classify in detail the diseases of women. Of the 49 cases

giving history of such diseases the following were noted: tubal and ovarian inflammation, pus-tubes, cystic ovary, endometritis, uterine fibroid, carcinoma of the uterus, displacement of the uterus, and pelvic inflammation. In a number of cases, symptoms referable to the genital tract were quite indefinite.

The feature of most interest and relative importance in the consideration of predisposing factors is the chronologic relationship of previous illness to the development of pellagrous symptoms. The following summary gives in some detail the information secured:

RECENT ILLNESS POSSIBLY PREDISPOSING TO PELLAGRA.

Gastric disturbance (including chronic gastric indigestion)	15
Dysentery (chronic during summer)	23
Diarrhea	6
Hookworm disease (moderate infection)	1
Ovarian cyst (large)	1
Uterine disease	4
General poor health (usually following childbirth)	30
Nephritis	3
Ascites (probably due to nephritis)	1
Valvular disease of the heart	1
Asthma	1
Pulmonary tuberculosis	7
Malarial fever	1
Alcoholism	1
Morphine habit	1
Infantile paralysis	1
Whooping cough	2
Measles	12
Chickenpox	1
No history of recent illness, 156	158
Health better than usual, 2	
<hr/>	
270	

In 15 of the cases a history of chronic indigestion was obtained. In explanation of these cases it may be said that symptoms of gastric disturbance preceded the active cutaneous symptoms of pellagra by a period of several months to several years. In 11 per cent. (30) of the cases no history of illness immediately preceding the development of pellagra could be obtained other than the fact that the general health was poor. Quite frequently this history of poor health followed confinement. One history of hookworm disease is included. This case showed objective clinical evidence of hookworm infection, which was uncommon for Spartanburg County. Malarial fever does not appear to be endemic in this county, and the one case included in this table was contracted in one of the "low country" counties. We were impressed with the fact that children not infrequently contracted pellagra during convalescence from acute infectious diseases, or very soon thereafter. It will be noted that 15 such observations were made: whooping cough, 2; measles, 12; chickenpox, 1. Of the 43 cases in children under ten years of age, 11 (approximately 23 per cent.) gave a

history of measles. In most of these the attack of pellagra occurred soon after recovery from measles.

SUMMARY. In the large majority of these cases (83 per cent.) economic conditions were poor, and the disease is most prevalent among people of insufficient means. We would, however, invite attention to the fact that 17 per cent. of these cases occurred in patients living in comfortable circumstances. This is not in agreement with Italian conceptions of the disease, where it presumably is confined altogether to the poorer element of the general population.

An analysis of general health conditions during childhood shows that in 86 per cent. of the cases the history was that of good health. So-called congenital diseases and inherited constitutional defects were of no apparent significance.

An analysis of diseases of adult life shows that in 25 per cent. of the cases, those giving a history of gastric disturbances, dysentery, and tuberculosis, a chronic disease was present, and it might be inferred that there is evidence of existing predisposition. During adult life the general health conditions were good in more than half the cases (62 per cent.).

An analysis of the obstetrical and gynecological data shows that among females who had reached the age of puberty, those most affected were married women (86 per cent.). As 86 per cent. of the married women had borne children and the average number of children borne was 3.8, it might be inferred that childbearing is an important predisposing factor. We know, however, that the average number of children borne by married women in the general population of the South is equal to or even greater than this.

Recent illnesses do appear to be worthy of serious consideration as predisposing factors, and it is our opinion that they frequently do influence not only the development of pellagra but also the severity of the attacks. It will be noted, however, that 59 per cent. of the cases in this series gave no history of illness immediately preceding the development of pellagra.

XV. STUDIES UPON HYGIENIC AND SANITARY CONDITIONS OF HOUSES AND PREMISES. *A. Houses.* The prevailing type of home in this county is a frame dwelling. The site usually is well drained, and there is always more than sufficient space between houses to afford free circulation of air.

In this study the dwelling houses are considered in three groups: brick, frame, and cabin.

Brick Dwellings. Dwellings of brick construction are relatively few in number. The mercantile houses in the larger centres are usually of brick construction, one or more stories in height, and the upper stories occasionally are used for living quarters. One of the cases included in this series was occupying such quarters.

Frame Dwellings. The mill-village dwellings are of the same general type, usually one story, sometimes two (Figs. 1, 2, 3, and 4).

The houses are almost always double. The single-story houses consist of a combination sitting and bed room, dining room, and

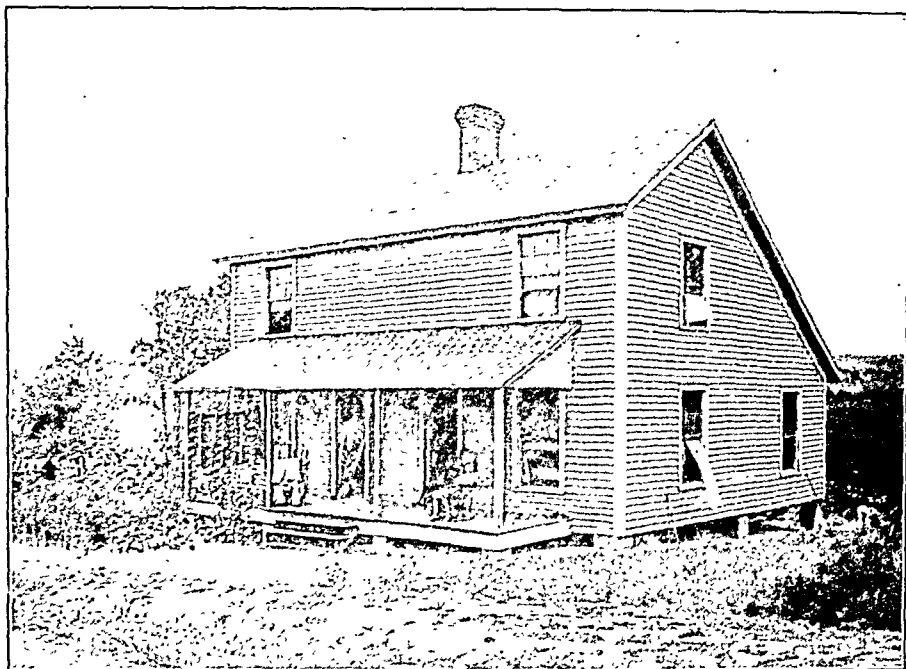


FIG. 1.—Typical mill-village house.

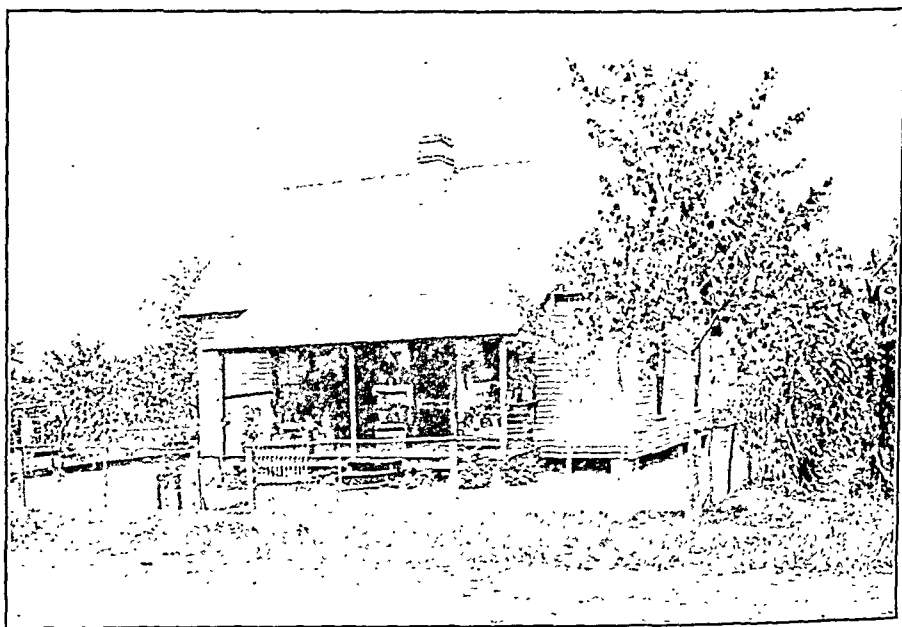


FIG. 2 —Typical mill-village house.

kitchen (Fig. 5). In the two-story houses there is in addition a bed room on the second floor. Small families occupy one-half

of a double single-story house, and large families live in either a two-story house or both sides of a double one-story house. There are two or three windows in each room and a small porch in front. These houses have no cellar, the foundation is brick, the ground floor is well above the ground, and the space between the ground

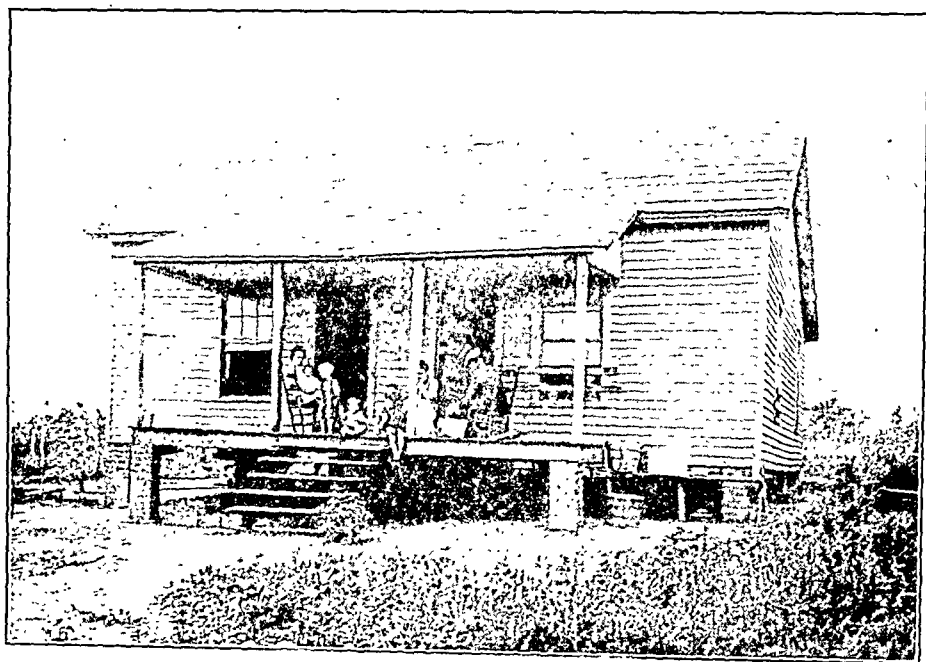


FIG. 3.—Typical mill-village house

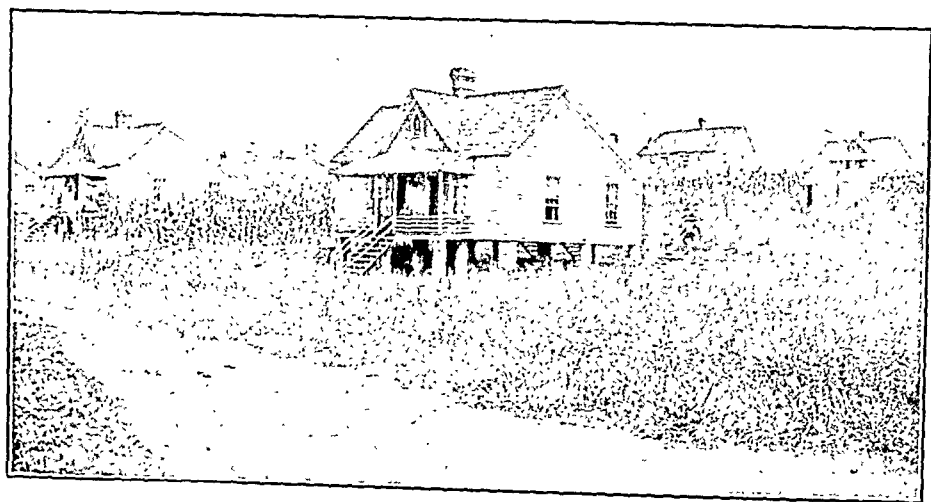


FIG. 4.—Typical mill-village house.

and ground floor is left open, permitting free circulation of air. Doors are placed directly in line from front to rear of the house, permitting free and unobstructed passage of fresh air. Rooms are sealed, both walls and ceiling. The timber used for this purpose is sometimes matched, sometimes not. The roof has a good pitch

with a large attic, permitting circulation of air, and the bed rooms have open fireplaces which further improve ventilation.

These houses are practically all infested with *Cimex*, and the grooves between the boards used in sealing the rooms afford an ideal place for the hatching out of broods of these insects.



FIG. 5.—Interior view, mill-village house.

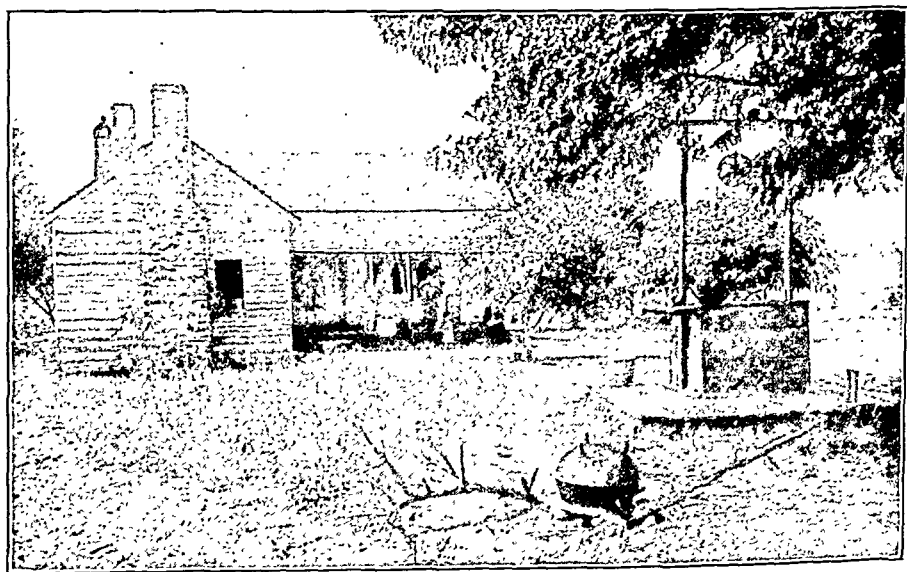


FIG. 6.—Type of farm-house and well.

The dwelling houses in the farming section are practically always frame houses (Fig. 6). Many of the farm-houses, more particularly

those occupied by owners, are well-constructed, roomy, and superior to the mill-village dwelling-house. On the other hand the usual tenant-house is inferior in many respects to that found in mill-villages.

Cabins. In this group are included the small frame or log dwellings, poorly constructed and ill-ventilated (Fig. 7). The negroes of the farming class usually occupy such houses.

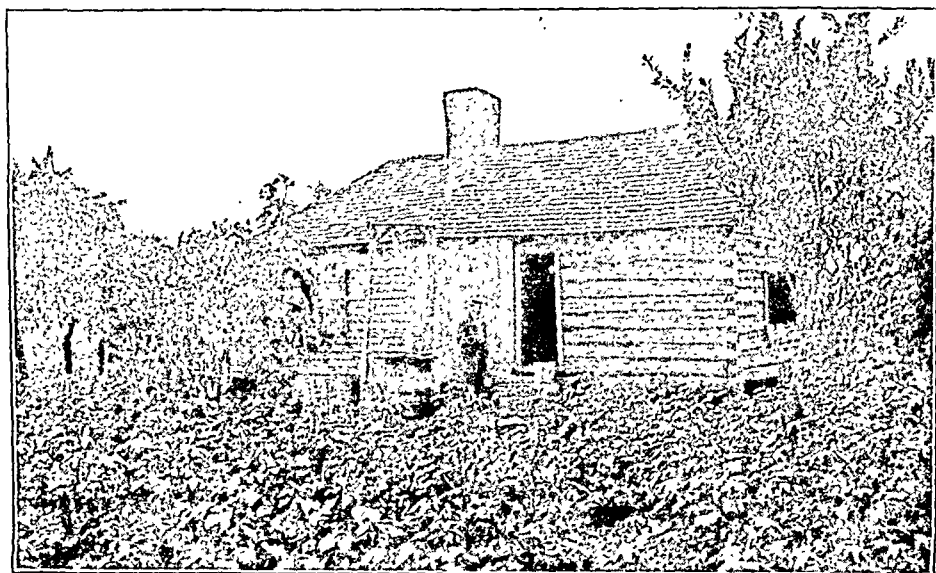


FIG. 7.—Type of cabin occupied by negro tenants on farms.

HYGIENIC AND SANITARY CONDITION OF HOUSES.

Brick	2
Frame	236
Cabin	19
	—
	257
Repair: Good	212
Poor	38
	—
	250
Screened: Yes	21
No	229
	—
	250
Ventilation: Good	155
Fair	86
Poor	8
	—
	249
General cleanliness: Good	142
Fair	92
Poor	12
	—
	246

SUMMARY. 92 per cent. of the cases lived in frame houses of fairly good size, and 85 per cent. of the houses investigated were in fairly good repair. Nine per cent. of the houses were screened, but in many instances the screening was more or less unsatisfactory. In only a small proportion of the screened houses did the screening afford satisfactory protection against the ingress of insects. *Musca domestica* was present in all, and *Stomoxys calcitrans* was present in many unprotected houses.

Ventilation. In 62 per cent. of the houses investigated, ventilation of the bed rooms was good, in 36 per cent. only fair, and in 3 per cent. poor. The number of persons occupying each bedroom averaged about three, and the available allowance of air space did not, in general, suggest overcrowding. Poor ventilation and overcrowded conditions were more in evidence in the negro population.

SUMMARY. We have failed to find anything of significance in connection with the houses from the standpoint of overcrowding and ventilation. It was observed that *Musca domestica* was always more or less abundant, and that of the blood-sucking insects, *Stomoxys calcitrans* and *Cimex lectularius* were of common occurrence. A detailed study of the observations on insects will be considered in the entomological section of this report.

B. Water Supply. The sources of water supply for drinking purposes among the general population of Spartanburg County are similar to those considered in this study. For analytical purposes the sources of supply are divided into three groups, wells, springs, and city water.

SOURCE OF WATER SUPPLY.

Wells: Dug well, with bucket	162		
Artesian well, with pump	30		192
Springs	13		13
City water, hydrant	36		36 241

PROTECTION OF WATER-SUPPLY WITH REFERENCE TO CONTAMINATION BY SURFACE WATER OR BY SEEPAGE AT POINT FROM WHICH SUPPLY IS DRAWN.

Protection satisfactory (water-supply drawn from hydrants, from artesian wells with concrete base, or from deep wells with concrete base)	65
Partly protected (water-supply drawn from wells with wooden base, either covered or uncovered, or from isolated springs)	176
	<hr/> 241

Wells. The wells are of several types. The type most common in rural districts and in some of the mill-villages is the ordinary dug well, about five feet in diameter (sometimes round and sometimes square), from thirty to sixty or more feet in depth, and protected at the top by a wooden frame. Though a few wells could be classified as "shallow wells," it was quite the usual thing to

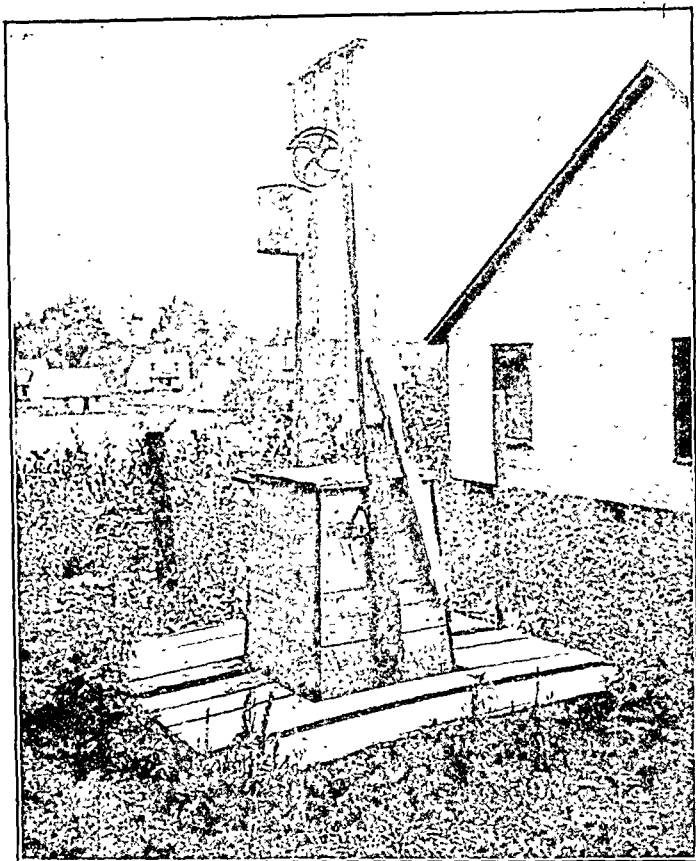


FIG. 8.—Typical dug well with bucket. Wooden base.

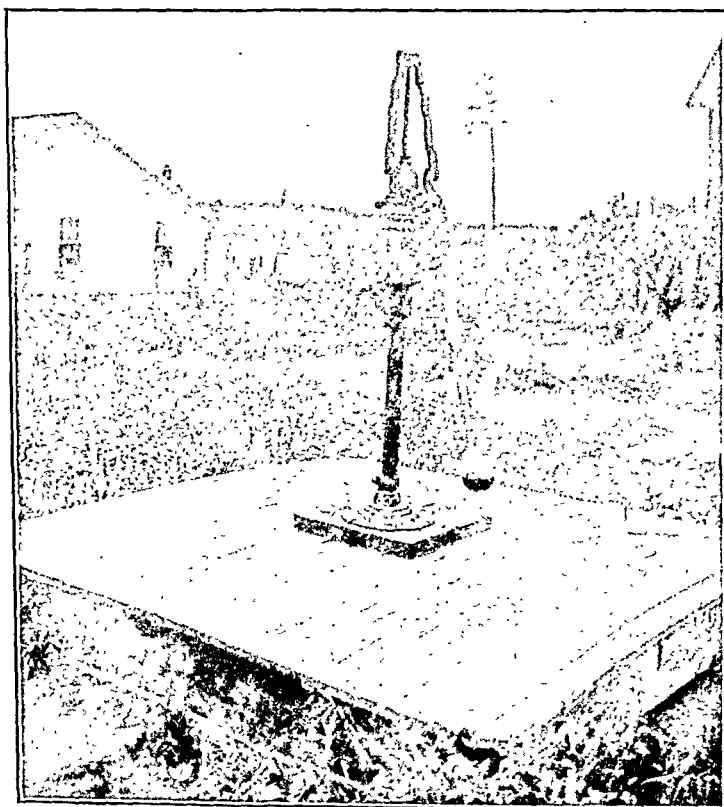


FIG. 9.—Type of driven pump well, wooden base.

find that the supply was obtained from a sufficient depth to insure that an impermeable stratum supervened, preventing contamination by surface water.

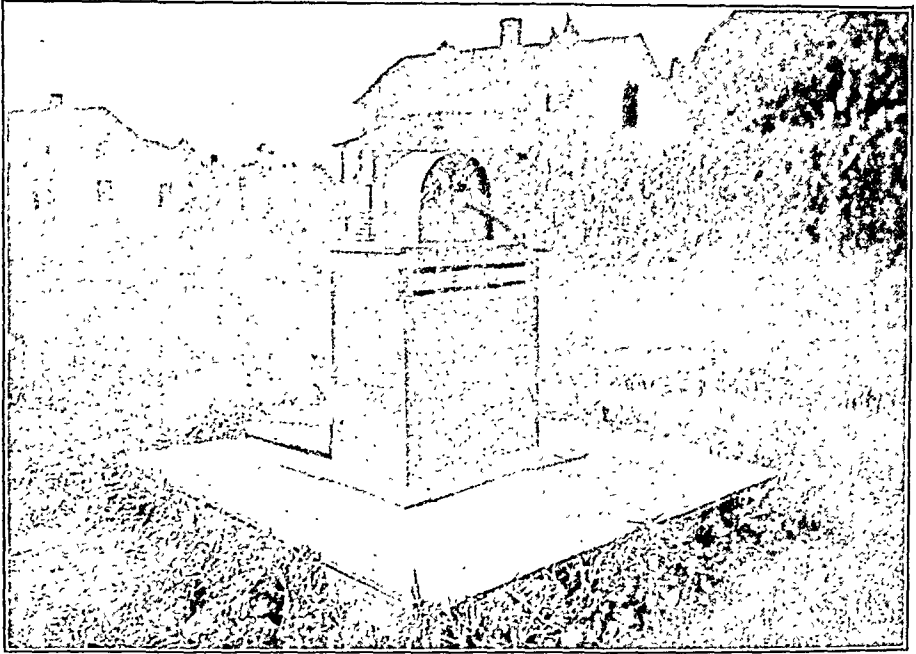


FIG. 10.—Type of bucket well, wooden base

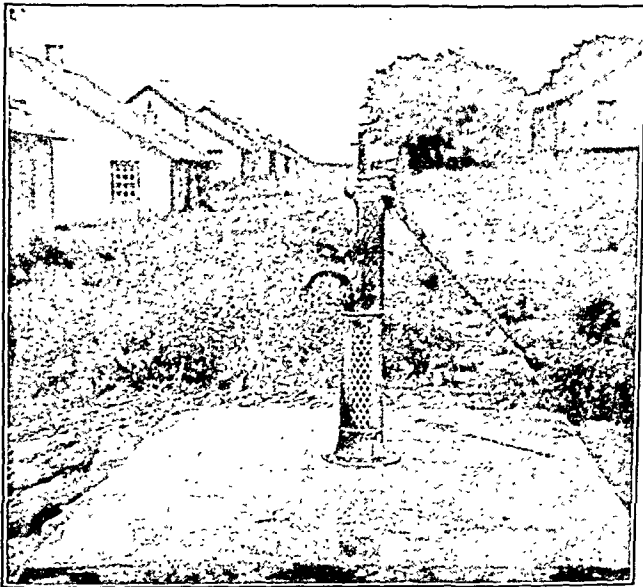


FIG. 11.—Type of driven well with pump. Sloping concrete base.

The water was usually drawn by means of the well-known bucket and windlass arrangement, but in a number of instances pumps were

in use. In the farming districts, ordinarily, no effort was made to guard against contamination at the immediate source of supply, but in some of the mill-villages these wells have concrete bases, sloping outward. The various types of wells can be better understood by reference to Figs. 8, 9, 10, 11, and 12.

In some of the mill-villages, artesian wells are in use. These artesian wells are usually quite deep, and the water is drawn by pump.

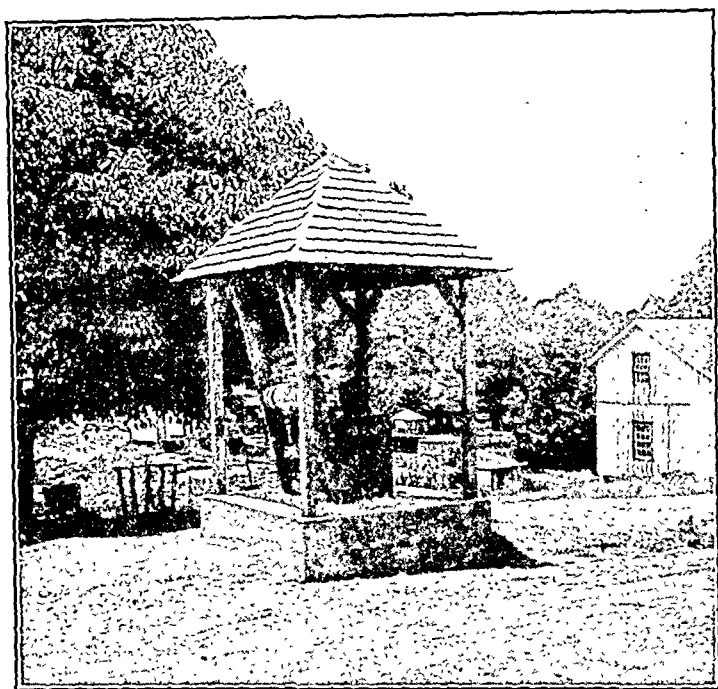


FIG. 12.—Dug well with bucket. Concrete base.

Springs. The use of spring water was, with one or two exceptions, confined strictly to the farming population living in comparative isolation. Usually drainage from the house was not in the direction of the spring, and the possibility of contamination was not a factor of importance.

City Water. This source of supply was confined to the city of Spartanburg. Bacteriological and chemical examinations are made from time to time, with no evidence of contamination.

SUMMARY. It will be noted that 80 per cent. of the cases used well water; 15 per cent. used city water; and 5 per cent. used spring water.

In 27 per cent. of the total observations (241) the water supply was perfectly protected from contamination. The remaining 73 per cent. are classified as partly protected, but this group requires some further explanation, as otherwise an erroneous inference might be drawn. We have included in this group all springs, all shallow wells, and all wells without a concrete base. As a matter

of fact, there were few shallow wells, and the probability of contamination in this group, considered as a whole, was but slight.

We realize that the water-supply is not considered to be of any importance as a factor in the etiology of pellagra. In this study, however, we have endeavored to investigate, as far as was possible, all probable factors concerned in the epidemiology of the disease, and for this reason have considered the water-supply. We have found nothing of any apparent significance in this connection.

C. Disposal of Excreta. In making a general survey of sanitary conditions, a study of the disposal of excreta was included. In classifying privy types we have adopted, for the sake of convenience, the classification used by the Rockefeller Sanitary Commission in its hookworm investigations in the Southern States.

INDEX OF PRIVY TYPES ADOPTED BY THE ROCKEFELLER SANITARY COMMISSION.

	Per cent.
Class A. Water carriage or Marine Hospital Barrel (L. R. S.)	100
Class B. Water-tight and rigidly fly-proof privy	75
Class C. Water-tight, closed-in back	50
Class D. Closed-in back, surface privy	25
Class E. Ordinary open-in-back surface privy	10
Class F. No privy	00

We encountered in this study one type of privy not falling strictly in any of these groups. The type in question (Fig. 14) was found in three or four of the mill-villages, and consisted of an out-house open in front and behind. The excreta were collected in square metal pails, supposedly water-tight. These pails were emptied at intervals. No attempt was made to keep out flies, the pails were frequently battered, and not water-tight, and usually were extremely filthy. It was not possible to include these privies in Class C, nor was it fair to put them in Class E. We have therefore placed them in Class D.

The following tables will show the facts observed:

PRIVY TYPES.

Class A	11
Class B	0
Class C	0
Class D	51
Class E	152
Class F	29
Total	243

SANITARY INDEX FOR ALL PRIVIES.

Class A. 11 at 100 per cent.	1100
Class B. 00 at 75 per cent.	00
Class C. 00 at 50 per cent.	00
Class D. 51 at 25 per cent.	1275
Class E. 152 at 10 per cent.	1520
Class F. 29 at 0 per cent.	00
Total	3895

Sanitary index = 16.

DISTANCE OF PRIVY FROM HOUSE.

10 yards	4
15 yards	9
20 yards	35
25 yards	25
30 yards	75
35 yards	4
40 yards	9
45 yards	1
50 yards	31
60 yards	2
70 yards	1
75 yards	1
100 yards	2
200 yards	1
Water-carriage system (Class A)	11
No privy (Class F)	29
Total	240

DISTANCE OF PRIVY FROM WELL.

10 yards	5
15 yards	5
20 yards	13
25 yards	7
30 yards	27
35 yards	7
40 yards	12
50 yards	45
60 yards	5
70 yards	6
75 yards	9
80 yards	1
85 yards	1
100 yards	5
110 yards	1
250 yards	1
Water-carriage system (Class A)	11
No privy (Class F)	29
Total	190

The cases in which the disposal of excreta was by water carriage (5 per cent.) were confined to the city of Spartanburg. No privy of the Marine Hospital type (L. R. S.) was observed. Between 30 and 40 cases of pellagra developed in the city of Spartanburg in other than mill-village sections. Only 8 of these cases used a water-carriage system of disposal of excreta. There were no privies of Class B or C. In 21 per cent. the privies were arbitrarily included in Class D. In 63 per cent. of the cases the method of disposal was that of the unhygienic and insanitary open surface privy, and in 12 per cent. of the cases no privy was used.

The method of disposal of excreta in the mill-villages, located in Spartanburg County falls under two classes, D and E (Figs. 13, 14, 15, 16, and 17): In some villages the pail system is in use, but beneficial results are negated by the fact that no effort is made to screen the closets properly either in front or behind. In other

villages the unhygienic open surface privy is in use, and flies have free access to large collections of excreta in close proximity to the dwelling-houses. In some mills the privies are cleaned weekly;

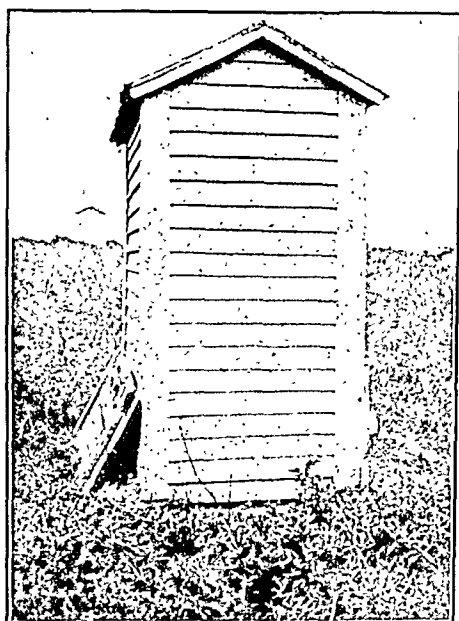


FIG. 13.—Privy, Type E. Surface, unscreened.

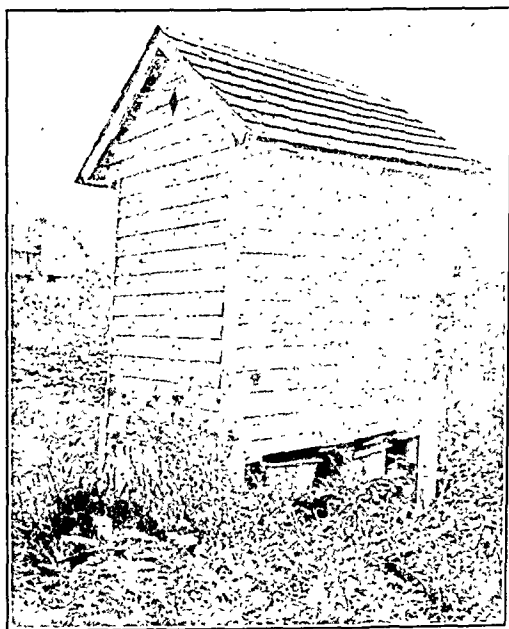


FIG. 14.—Privy, Type D. Pail system, unscreened.

in others, at greater and more irregular intervals. In some villages the sanitary condition around the privies is extremely poor, while in others some attempt is made to keep things relatively clean.

In the farming districts the methods of disposal fall in Classes E and F (Fig. 18). The open-surface privies on farms usually are

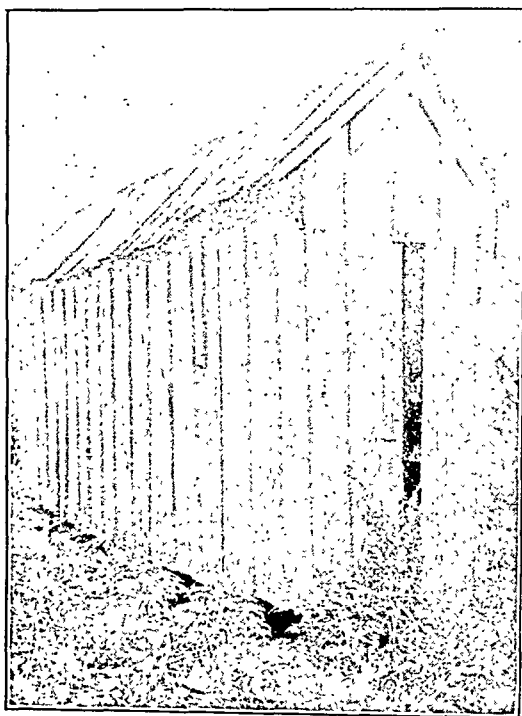


FIG. 15.—Privy, Type E. Surface, unscreened.

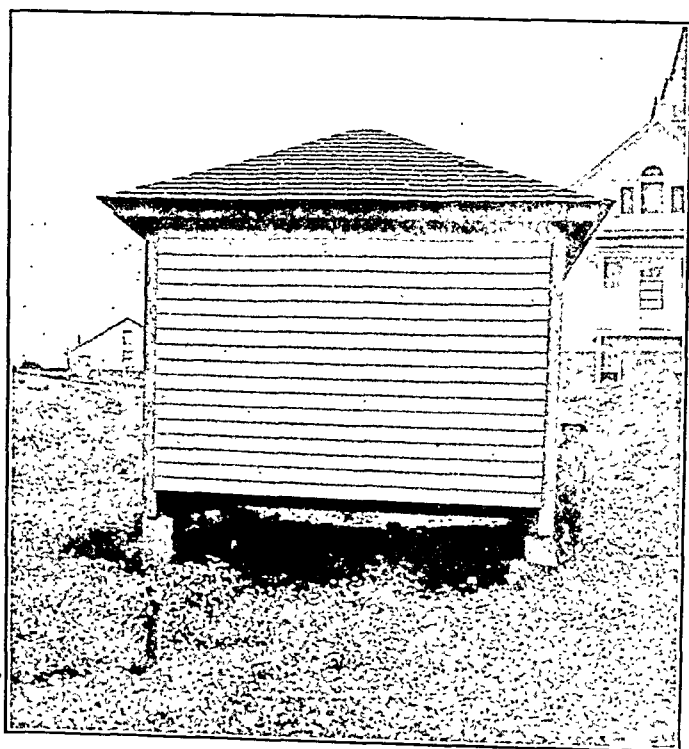


FIG. 16 —Privy, Type E. Surface, unscreened

poorly constructed and filthy, and the excreta are seldom removed, poultry being relied upon as scavengers. Negroes in the farming



FIG. 17.—Privy, Type E. Surface, unscreened.



FIG. 18.—Privy, Type E. Surface, unscreened, on farm.

districts seldom have privies, and we were greatly surprised to find that farmers of the better classes sometimes had no privies.

The methods of disposal of excreta observed by us among the families of pellagrins in the different groups of the population are similar to the methods of disposal adopted by the general population in these groups.

Many of the mill authorities are well aware of the importance of good sanitation, and it is their constant endeavor to improve conditions. Even now plans are under way for the installation of a water-carriage system of disposal in one or two of the larger and better mills.

SUMMARY. The average general sanitary index for all the privies studied is only 16, on a basis of 100 for perfect disposal. So far as population groups are concerned the methods of disposal in use by the general population are not different from those observed among pellagrous families. Between 30 and 40 cases of pellagra developed in the city of Spartanburg more or less away from mill districts, and only 8 of these cases used a water-carriage system of sewage disposal. In general the methods of disposal of excreta observed in this series are insanitary, and many of the diseases of the intestinal canal transferred by mechanical means, flies, etc., would find conditions most favorable for such transfer.

D. Premises. The following table covers the observations made relative to the sanitary conditions of the premises of pellagrins:

LOCATION OF HOUSE RELATIVE TO MOISTURE AND DAMPNES.	
Air and soil:	Dry 242
	Damp 6—248
Drainage:	Good 242
	Poor 6—248
General cleanliness of premises:	Good 146
	Fair 90
	Poor 12—248
Stagnant water:	Yes 7
	No 239—246
Shade:	None 145
	Little 62
	Much 38—245
Undergrowth or shrubbery:	None 207
	Little 36
	Much 2—245
Barns:	Number of houses having barns 90
	Number of houses having no barns 145—235
Animal: ¹⁵	Dogs 76
	Cats 79
	Horses or mules 54
	Cows 93
	Goats 6
	Fowl 158
	Rats 88
	Mice 124

¹⁵ Number of observations, 237.

SUMMARY. In 98 per cent. of the cases the dwelling-houses were well located and the drainage was good. Stagnant water was noted on the premises in only 3 per cent. of the houses investigated (246). But few mosquitoes were observed. The entomological section of this report will deal with permanent streams and collections of water, with the blood-sucking insects breeding therein, and with other biting insects found in the houses, on the premises, and in the neighborhood.

XVI. GENERAL OBSERVATIONS UPON THE DIETARY. The data analyzed in this study are necessarily of a general nature, based on information obtained from statements of patients, physicians, storekeepers, millers, and others.

In order to determine the relative frequency with which the more important foodstuffs were used, patients and their families were closely questioned as to how often certain articles of food would appear upon the family table, and with regard to the patient's particular fondness for any particular dish. Replies to these questions were recorded under the following heads: Daily, one or more times a day; habitually, one or more times a week, but not daily; rarely, at irregular intervals of more than a week; never.

With a view to discovering any significant differences in the habitual dietary of the three groups in the population which show the greatest disparity in the prevalence of pellagra, the results of this inquiry are summarized for the rural population, urban population, and the mill-village population, separately. These results are set forth in the following tables, which represent the actual number of pellagrins and the percentage of the total number of pellagrins from whom the particular information in question was obtained.

TABLE XI.

FRESH MEATS:			Daily.	Habit- ually.	Rarely.	Never.
Fresh beef in season	Mill popula- tion	Number	1	51	84	11
		Per cent.	1	35	57	7
	Urban popula- tion	Number	3	27	16	0
		Per cent.	7	59	34	0
	Rural popula- tion	Number	2	20	40	12
		Per cent.	3	27	54	16
Fresh pork in season	Mill popula- tion	Number	9	68	60	10
		Per cent.	6	46	41	7
	Urban popula- tion	Number	1	33	12	0
		Per cent.	2	72	26	0
	Rural popula- tion	Number	4	45	18	5
		Per cent.	5	63	25	7
Fresh fish in season	Mill popula- tion	Number	0	32	79	34
		Per cent.	0	22	55	23
	Urban popula- tion	Number	0	14	29	2
		Per cent.	0	31	64	5
	Rural popula- tion	Number	0	7	44	21
		Per cent.	0	10	61	29

TABLE XI.—Continued.

			TABLE XI.—Continued.			
			Daily.	Habit- ually.	Rarely.	Never.
FRESH MEATS:						
Fresh fowl in season	Mill popula- tion	Number	1	59	81	6
		Per cent.	1	40	55	4
	Urban popula- tion	Number	1	30	14	2
		Per cent.	2	64	30	4
	Rural popula- tion	Number	2	45	23	2
		Per cent.	3	62	32	3
CURED MEATS:						
Cured beef	Mill popula- tion	Number	1	0	25	94
		Per cent.	1	0	21	78
	Urban popula- tion	Number	0	1	10	26
		Per cent.	0	3	27	70
	Rural popula- tion	Number	0	1	3	66
		Per cent.	0	1	4	95
Cured pork	Mill popula- tion	Number	92	40	10	2
		Per cent.	64	28	7	1
	Urban popula- tion	Number	25	9	9	2
		Per cent.	56	20	20	4
	Rural popula- tion	Number	49	12	8	1
		Per cent.	70	17	12	1
Cured fish	Mill popula- tion	Number	1	6	45	95
		Per cent.	1	4	31	64
	Urban popula- tion	Number	1	5	15	22
		Per cent.	2	12	35	51
	Rural popula- tion	Number	1	3	14	53
		Per cent.	1	4	20	75
Canned beef	Mill popula- tion	Number	0	14	80	51
		Per cent.	0	10	55	35
	Urban popula- tion	Number	0	3	20	20
		Per cent.	0	7	47	46
	Rural popula- tion	Number	0	2	25	46
		Per cent.	0	3	34	63
Canned pork	Mill popula- tion	Number	0	7	39	88
		Per cent.	0	5	29	66
	Urban popula- tion	Number	0	2	14	24
		Per cent.	0	5	35	60
	Rural popula- tion	Number	0	1	7	58
		Per cent.	0	2	11	87
Canned fish	Mill popula- tion	Number	0	20	90	30
		Per cent.	0	14	64	22
	Urban popula- tion	Number	1	7	28	8
		Per cent.	2	16	64	18
	Rural popula- tion	Number	0	5	38	29
		Per cent.	0	7	53	40
EGGS, BUTTER, AND MILK:						
Eggs	Mill popula- tion	Number	10	36	13	2
		Per cent.	16	59	22	3
	Urban popula- tion	Number	7	8	0	0
		Per cent.	47	53	0	0
	Rural popula- tion	Number	11	12	17	3
		Per cent.	25	28	40	7
Butter	Mill popula- tion	Number	114	16	12	4
		Per cent.	78	11	8	3
	Urban popula- tion	Number	33	6	8	0
		Per cent.	70	13	17	0
	Rural popula- tion	Number	51	8	9	6
		Per cent.	69	11	12	8
Milk	Mill popula- tion	Number	83	21	29	12
		Per cent.	57	15	20	8
	Urban popula- tion	Number	16	14	16	9
		Per cent.	29	25	29	17
	Rural popula- tion	Number	41	15	18	9
		Per cent.	49	18	22	11

TABLE XI.—Continued.

VEGETABLES, FLOUR, LARD:			Daily.	Habit- ually.	Rarely.	Never.
Fresh vegetables in season	Mill popula- tion	Number	120	21	3	3
		Per cent.	82	14	2	2
	Urban popula- tion	Number	36	6	4	0
		Per cent.	78	13	9	0
	Rural popula- tion	Number	61	11	1	0
		Per cent.	84	15	1	0
Canned vegetables	Mill popula- tion	Number	4	41	70	29
		Per cent.	3	28	49	20
	Urban popula- tion	Number	2	17	25	2
		Per cent.	4	37	54	5
	Rural popula- tion	Number	3	8	25	37
		Per cent.	4	11	34	51
Wheat flour	Mill popula- tion	Number	142	1	0	0
		Per cent.	99	1	0	0
	Urban popula- tion	Number	45	0	0	0
		Per cent.	10	0	0	0
	Rural popula- tion	Number	71	1	0	0
		Per cent.	99	1	0	0
Leaf lard (pork)	Mill popula- tion	Number	30	16	2	0
		Per cent.	62	34	4	0
	Urban popula- tion	Number	10	2	0	0
		Per cent.	83	17	0	0
	Rural popula- tion	Number	28	4	0	0
		Per cent.	87	13	0	0
Compound lard	Mill popula- tion	Number	101	2	23	5
		Per cent.	77	2	18	3
	Urban popula- tion	Number	37	5	2	1
		Per cent.	82	11	5	2
	Rural popula- tion	Number	62	1	7	1
		Per cent.	87	1	10	2

TABLE XII.

CORN PRODUCTS. CORN MEAL USED.

		Daily.	Habitually.	Rarely.	Never.
Mill population	Number	85	21	40	0
	Per cent.	58	14	28	0
Urban population	Number	23	12	10	2
	Per cent.	49	26	21	4
Rural population	Number	47	13	11	0
	Per cent.	66	18	16	0

SOURCE OF SUPPLY OF MEAL. SHIPPED MEAL GROUND IN NEARBY STATE

		Exclusively.	Mostly.	Rarely.	Never.
Mill population	Number	84	8	22	4
	Per cent.	71	7	19	3
Urban population	Number	29	2	5	1
	Per cent.	78	5	14	3
Rural population	Number	16	9	13	4
	Per cent.	38	21	31	10

LOCAL CORN GROUND LOCALLY.

		Exclusively.	Mostly.	Rarely.	Never.
Mill population	Number	30	22	2	0
	Per cent.	56	40	4	0
Urban population	Number	7	7	0	0
	Per cent.	50	50	0	0
Rural population	Number	32	19	4	0
	Per cent.	58	35	7	0

TABLE XII.—Continued.

QUALITY OF MEAL.

		Good.	Musty.
Mill population	Number	41	49
Urban population	Number	13	12
Rural population	Number	34	18

USE OF HOMINY OF GRITS.

		Daily.	Habitually.	Rarely.	Never.
Mill population	Number	9	47	53	19
	Per cent.	7	37	41	15
Urban population	Number	9	16	7	5
	Per cent.	24	43	19	14
Rural population	Number	5	14	23	11
	Per cent.	10	26	43	21

		Syrup.	Corn-starch.	Whisky.
Mill population	Number	47	5	19
	Per cent.			
Urban population	Number	23	5	9
	Per cent.			
Rural population	Number	27	3	6
	Per cent.			

Meats. The following meats were used to a greater or less extent in these three subdivisions of the population: fresh meat, fresh pork in season, fresh fish in season, fresh fowl, dried or chipped beef, bacon, cured fish, canned beef, canned sausages, and canned salmon. Fresh beef is not a staple article of diet of any of these population groups during the summer months. By far the greater number of individuals among the mill-village and rural population groups used it but rarely, and some never, while the urban group used it more extensively. The actual percentages of those eating fresh meat, either rarely or never, are as follows: Rural cases, 70 per cent.; mill-village cases, 64 per cent.; urban cases, 34 per cent. Fresh pork in season was used approximately equally in the three groups, but rather more generally in the rural group, the actual percentages of those using it daily or habitually being as follows:

Urban cases, 74 per cent.; rural cases, 68 per cent.; mill-village cases, 52 per cent.

Fresh fish is not a common article of diet in Spartanburg County, and was but rarely used in any of the three groups. This statement applies more particularly to the mill-village and rural population. The percentages of those using fresh fish either rarely or never are as follows: urban cases, 59 per cent.; rural cases, 90 per cent.; mill-village cases, 78 per cent.

Fresh fowl was used quite extensively in all three groups particularly during the summer months; most extensively by the rural

cases; less so by the urban group, and least extensively by the mill-village group. The actual percentages of those using fowl, either daily or habitually, are as follows: urban cases, 66 per cent.; rural cases, 65 per cent.; mill-village cases, 41 per cent.

Cured beef is used but rarely in any of the three groups. In 95 per cent. of the rural group, 78 per cent. of the mill-village group, and in 70 per cent. of the urban group it was never used.

Bacon (cured pork) is a common article of diet in all groups, being used either daily or habitually by 92 per cent. of the mill-village group, 87 per cent. of the rural group, and 76 per cent. of the urban group.

Cured fish is little used in any of the three groups, though somewhat more frequently in the city population than by the other two classes.

Canned beef is not used extensively. In 63 per cent. of the rural cases, 46 per cent. of the urban cases, and 35 per cent. of the mill-village cases it is never used. When used it appears to be eaten neither daily nor habitually.

Canned sausages (pork) are quite extensively used although seldom with any great frequency or regularity. The farming population uses them least.

Canned Fish. Canned salmon, while quite generally used, is not a staple article of diet in any of the groups. In 93 per cent. of the rural cases, 86 per cent. of the mill-village cases, and 82 per cent. of the urban cases it is rarely or never used.

Eggs, Butter, and Milk. These farm and dairy products are used with great frequency and regularity in all three groups of the population. Eggs were used either daily or habitually by 100 per cent. of the urban cases, 75 per cent. of the mill-village cases, and 53 per cent. of the rural cases. Butter was used daily or habitually by 89 per cent. of the mill-village cases, 83 per cent. of the urban cases, and 80 per cent. of the rural cases. Milk was used either daily or habitually by 72 per cent. of the mill-village cases, 67 per cent. of the rural cases, and 54 per cent. of the urban cases. The use of eggs and butter is not so common in the rural group as in the other two. It must be remembered, however, that a greater number of negroes are included in this group, and their diet is probably below that of the whites, more particularly from the standpoint of variety. For example, Table XI shows that in 3 cases among the rural population, eggs were never used; 2 of these cases were negroes. Of 6 cases that never used milk, 3 were negroes. Our data are not sufficiently extensive to draw a careful comparison between the average dietary of whites and negroes at the present time. Further information on this subject will be sought the coming season.

Vegetables. Fresh vegetables were used in season, to a very large extent, by all the groups. They were used either daily or habitually

by 99 per cent. of the rural cases, by 96 per cent. of the mill-village cases, and by 91 per cent. of the urban cases. Among the vegetables most commonly used may be mentioned cabbages, green corn, beans, potatoes (Irish and sweet), peas, tomatoes, and squash. During the winter months the available vegetables were confined largely to Irish potatoes, cabbage, peas, and beans. Canned vegetables were seldom used habitually. In 85 per cent. of the rural cases, 69 per cent. of the mill-village cases, and 59 per cent. of the urban cases they were either rarely or never used.

The lards used consisted of pure leaf lard, the compound lards, and pure vegetable (cotton-seed) lards. In 7 cases pure leaf (hog) lard was used exclusively. In many instances, particularly so in the rural cases, sufficient lard was rendered from the pork killed at home to supply all needs for from two to eight months of the year or longer. Others used compound or pure vegetable lards exclusively. Inquiry among 50 non-pellagrous families in one mill-village showed the use of compound lards to be quite as extensive as among pellagrins.

Some of the grocers catering to the well-to-do classes of the population in Spartanburg informed us that some customers preferred the pure leaf lard, while others preferred and used constantly the pure vegetable lards.

Wheat Flour. Bread made of wheat flour was used daily by 99 per cent. of the cases in each group, and was used habitually by the remaining 1 per cent.

Corn Products. Among the corn products used are included corn meal, hominy, grits, syrup, corn-starch, and whisky. Corn-meal is a staple article of diet in all classes of the population in the area studied. In this series, 84 per cent. of the rural cases, 75 per cent. of the urban cases, and 72 per cent. of the mill-village cases used corn-meal either daily or habitually. Two cases had not used corn-meal for a period of two years prior to the development of pellagra. These cases were two children whose mother had contracted pellagra in 1910, at which time she was advised by her physician to discontinue the use of corn products absolutely. She states that she had done so and that there had been no corn products in the house for the past two years. The children, aged six and thirteen years respectively, developed the disease in 1912.

The meal was obtained from different sources. Many of the families used no meal other than that grown locally and ground at a local mill; others used such meal the greater part of the time; others used, exclusively, meal shipped in from a near-by state; and still other used such meal the greater part of the time, but used more or less meal made from local corn, locally ground. The cases in which both local and shipped meal was used are included in both tables, which accounts for the apparent excess in numbers.

Some families raised sufficient corn to supply them with meal,

locally ground, for from six to eleven months of the year, the remainder being purchased from a grocer. The quality of the meal varied. When meal was made from the home-raised corn it was the usual custom to grind it up in small amounts at frequent intervals, and such meal was said to be fresh and sweet. The meal purchased from grocers was sometimes musty, but such meal usually was fed to the chickens. The use of hominy and grits was not so common in these groups as had been expected. Among the rural cases 64 per cent., the mill-villages cases 56 per cent., and the urban cases 33 per cent. rarely or never used either.

Comparative dietary studies on the normal non-pellagrous population under like conditions are desirable in any attempt to determine the possible influence of the dietary on the development of pellagra. We have made some comparative studies with this object in view, but our data are not sufficiently complete at this time to warrant any definite conclusions.

The diet to which most of these cases were accustomed is of fairly good variety, but it is probable that in many instances the methods of preparation and cooking of the food are subject to criticism. This matter likewise is to be made a subject of further investigation. We are quite certain, from personal observation, that the average dietary of the poorer classes of the population in the county studied is much superior both in its variety and actual nutritive value to the dietary of the peasants in the North of Italy. Another striking difference may be mentioned, namely, that corn-meal in the form of polenta constitutes the chief bread component of the diet of the peasant of Northern Italy, whereas in Spartanburg County, among all classes of the population, wheat flour, in the form of bread or biscuit, is the principal bread-stuff, and corn-meal, while extensively used, is not nearly so staple an element of the dietary as wheat flour.

XVII. SYNOPSIS. The epidemiological study of pellagra as it exists in Spartanburg County, South Carolina, is still in progress and will be continued during the spring and summer of 1913. The work done in 1912 constituted a more or less general preliminary survey of the field, and the results of that work as set forth in this report are tentative and will be further tested by continued observations and study.

The results of the work in 1912 tend to strengthen the belief that a satisfactory knowledge of the epidemiology of pellagra is best to be gained by intensive studies, of the behavior of the disease in selected communities, and of the prevailing conditions which influence its local prevalence and distribution. It is hoped that a study conducted with sufficient care and thoroughness along these lines will yield valuable evidence either for or against the possible infectious nature of the disease and its possible communicability.

The epidemiological data presented in the present report are summarized below:

PART I. 1. Pellagra shows a striking inequality of distribution in the ten townships within the county, the township rate of prevalence per 10,000 of population varying from 0 to 71. The city of Spartanburg, with a population of 17,517 gave a rate of 49 per 10,000 against 34 per 10,000 for the remainder of the county.

2. Density of population while showing a tendency to conform to the relative prevalence of the disease does not alone offer an explanation of the geographical inequalities of its distribution within the county.

3. The cotton-mill-village population gives a rate of prevalence of 104 per 10,000 against 19 per 10,000 for the remainder of the county, and against 16 per 10,000 for the rural sections alone.

4. The variations in the rates of prevalence in the ten townships are in a measure proportional to the presence or absence of a large mill-village population. Excluding the mill-village population, there is still a marked discrepancy between the townships in the rural population alone, ranging from 0 to 29 cases per 10,000 of population. The excessive prevalence among the farming classes is found in the townships which have a relatively large mill-village population.

5. The white population of the county gives a prevalence of 45 cases per 10,000; the negro population a prevalence of 9.5 per 10,000. Excluding the mill-village population which is practically all white, the remaining white population still gives a rate of prevalence (25.2 per 10,000) over two and one-half times that among the negroes.

6. The rate of prevalence per 10,000 for males in the county is 17; for females, 50.5. White males give a rate of 22.95 per 10,000; white females, 87.5 per 10,000, negro males, 3.9 per 10,000; negro females, 14.9 per 10,000.

7. The rate of prevalence among children under ten years of age and among adults aged forty-five years and older is practically equal in the two sexes.

8. The rate of prevalence drops among males between the ages of nineteen and forty-five years, whereas for females there is a remarkable excess of prevalence between these ages.

9. In both males and females there is a striking fall in prevalence between the ages of ten and twenty years.

10. The most significant fact with regard to occupation is the excessive prevalence of pellagra among women employed in house-work.

11. The excessive prevalence of pellagra in the mill-village population is found largely among women and children at home during the day. Among actual mill-workers the rate of prevalence between the two sexes appears to be about equal.

12. One-half of the cases occurred singly in one family; about one-fourth occurred two in one family; the remaining fourth occurred in groups of three, four, or five in one family. The question of the possible relative importance of family relationship and household association is still under investigation.

13. Among cases occurring singly in families, the proportion of children of both sexes under ten years of age is low and that of adult females excessively high. Among cases occurring two or more in one family the proportion of young children is proportionately high, especially among males.

PART II. 14. While apparently authentic sporadic cases of pellagra within the county can be traced back to as early as 1894, the disease does not appear to have occurred in any great number of cases in any year until 1908. Since 1908 the incidence-rate appears to have rapidly increased each year to 1911. The number of new cases developing in 1911 appears to have been slightly greater than in 1912.

15. There was no evidence pointing to any spring and fall recrudescence of the disease in the population so frequently referred to in the literature of pellagra. There is no particularly marked tendency for the seasonal recurrence to appear in an individual during the same month, year after year.

16. *Influence of Climate.* Climatic conditions appear to influence the development of symptoms of the disease. If during the spring months precipitation is high, temperature low, and number of rainy days excessive, the appearance of acute symptoms, more particularly those involving the skin, is delayed.

17. *Symptomatology.* It would appear that three or four years ago a large proportion of the cases observed in the county presented intestinal and nervous symptoms of great severity. In 1912, in many instances, symptoms were quite mild, and sometimes were confined almost exclusively to the cutaneous system, the disease appearing to be of a less virulent type in 1912 than in previous years.

18. *Economic Status.* In the majority of cases (83 per cent.) economic conditions are poor and the disease is most prevalent among people of insufficient means.

19. *Predisposing Diseases.* General health conditions in childhood do not appear to warrant consideration as etiological factors when the disease develops in adult life. In a number of cases the development of pellagrous symptoms in children was preceded by one of the acute exanthematous diseases of childhood. About one-fourth of the cases gave a history of a preceding chronic disease in adult life. In more than one-half of the cases (62 per cent.) the history was that of good health. Among adult females, those most affected were married women (86 per cent.), and 86 per cent. of the married women had borne children.

A history of illness immediately preceding the development of pellagra was elicited in 59 per cent. of the cases.

20. *Hygiene and Sanitation of Houses and Premises.* The most unsanitary condition found in the county is the absence of properly constructed privies. Outside of a part of the city of Spartanburg which is supplied by a water-carriage sewage system, there is no effective provision in the county for the proper disposal of human excreta. A second striking unsanitary condition is the almost complete absence of effective screening of dwellings.

These two conditions present a situation highly favorable to the transmission of disease organisms eliminated in the excreta, both by direct contamination of food and person and by insects. This situation is naturally aggravated in the mill-villages and small towns by the greater congestion of houses. The absence of effective screening for dwellings gives rise to conditions conducive to the possible transfer of diseases transmitted by biting insects.

21. *Dietary.* Observations upon the habitual use of the more common foodstuffs failed to discover any points of difference between pellagrins and non-pellagrins in the county or any facts which would seem to explain the strikingly greater prevalence of pellagra among certain classes of the population.

The most striking defect in the general dietary of the working classes, appears to be the limited use of fresh meats, the animal proteid being supplied largely in the form of cured meats, of which salt pork (especially bacon) is the most important.

Unhygienic preparation of food appears to be a probable important factor in the general health of the population.

Investigation of the kind, quantity, and quality of corn and corn products used in the county failed to bring to light any epidemiological evidence pointing to the agency of corn as an etiological factor in the disease. The presence of two cases in our series giving a definite history of no corn consumption within two years prior to the onset of symptoms, together with several other cases in which corn products were eaten, if at all, only in small quantity and at extremely rare intervals, would seem to argue strongly against any hypothesis that corn products alone are the causative agent of the disease.

REVIEWS

MANUAL OF CHEMISTRY. A GUIDE TO LECTURES AND LABORATORY WORK FOR BEGINNERS IN CHEMISTRY. A TEXT-WORK SPECIALLY ADAPTED FOR STUDENTS OF MEDICINE, PHARMACY, AND DENTISTRY. By W. SIMON, PH.D., M.D., Professor of Chemistry in the College of Physicians and Surgeons of Baltimore and in the Baltimore College of Dental Surgery; Emeritus Professor in the Maryland College of Pharmacy, Department of the University of Maryland, and DANIEL BARE, PH.D., Professor of Chemistry in the Maryland College of Pharmacy, Department of the University of Maryland, and of Analytical Chemistry in the Department of Medicine, University of Maryland, Baltimore. Tenth edition, thoroughly revised, with 82 illustrations, 1 colored spectra plate and 8 colored plates representing 64 chemical reactions. Philadelphia: Lea & Febiger.

THE many editions through which Simon's *Manual of Chemistry* has passed, render somewhat superfluous on the reviewer's part more comment than is necessary to point out where the present edition differs from its predecessors. There may be honest difference of opinion as to the wisdom of attempting to compass within one volume, the subjects of Physical Chemistry, Inorganic Chemistry, Analytical Chemistry, Organic Chemistry, and Physiological Chemistry, but this difference evidently does not extend to those for whom the book is primarily intended. Ten editions of any work indicate its popularity with its chosen audience.

The authors have preserved in this the plan and characteristics of previous issues but have made many additions to the text, embracing such topics as exothermic and endothermic reactions; the theory of electrolytic dissociation and ionization, on which are based our present conceptions of the reactions of the body fluids; reversible reaction and chemical equilibrium; the chemistry of atoxyl, salvarsan, fluorescin, phenolsulphonephthalein, etc. In their own words the aim of the authors has been "to furnish the student in concise form a clear presentation of the science, an intelligent discussion of those substances which are of interest to him and a trustworthy guide to his work in the laboratory." In this they may fairly be said to have succeeded and many readers whose equipment in chemistry is rusty or has never

included the modern advances, will find here a simple and clear, if not complete, exposition of the subject.

The type is large and the wood cuts fulfil their purpose as illustrations. R. P.

SURGERY, ITS PRINCIPLES AND PRACTICE, BY VARIOUS AUTHORS.

Edited by WILLIAM WILLIAMS KEEN, M.D., LL.D., Emeritus Professor of the Principles of Surgery and of Clinical Surgery, Jefferson Medical College, Philadelphia. Volume VI; pp. 1177; 519 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THIS is a supplementary volume, designed to bring up to date the various chapters contained in the original five volumes of the work, which were published between 1906 and 1909. There are very few topics to which no additions have been made, owing to the rapid advance in surgical practice; and some entirely new subjects have presented themselves for discussion. Among the more important of the latter are Crile's principle of anoci-association, the surgery of the hypophysis, and modern thoracic surgery.

The most interesting additions to the principles of surgery are the explanation given by Adami of the value of poultices in favoring the pointing of an abscess, and his description of the use of cell proliferants, of Scharlach R., and of allantoin. In similar vein is Freeman's discussion of the treatment of abscesses by ferments and antiferments. Such matters as these remind us that progress occurs in the science as well as in the art of surgery.

T. Turner Thomas has prepared the supplementary chapter on surgical tuberculosis. He discusses the treatment with tuberculin, the uses of the formalin-glycerin solution, which should never be *less* (not more) than twenty-four hours old when used; and he makes brief but rather inadequate mention of tuberculous rheumatism. This, as well as the broader subject of inflammatory tuberculosis, merits wider attention than it has heretofore received outside of France.

In the supplementary chapter on Orthopedic Surgery it is very surprising to find that Lovett dismisses the bone transplantation for Pott's Disease (Albee) as a method still on trial, and that no mention whatever is made of one of the most revolutionary practices ever introduced into any department of surgery, namely, the Abbott treatment of scoliosis.

Dean D. Lewis and Kanavel contribute a chapter of fifty pages on the surgery of the hypophysis. Its comprehensiveness may be indicated by the statement that much of it is in small print, and that the bibliography alone covers three pages.

Owen supplements his original article on the surgery of the neck by giving the technique of operations for malignant disease in this region; but he does not commit himself as to whether or not the operation, when it involves the mouth, should be completed in one or in two sittings. He quotes Braun's experiences in performing some of these most radical operations under anesthesia by infiltration of the branches of the trigeminal nerve with cocaine; but he concludes that while Braun's essay is an attractive one, it is not altogether convincing to a surgeon like Owen himself who has a dread of the risks of cocaine poisoning.

Murphy, like everyone else, is theoretically awake to the advantages of the transverse incision in the lateral regions of the abdominal wall. He mentions the contributions of both Rockey and Hesselgrave, but fails to credit J. W. Elliot, or G. G. Davis, or Chaput for their original work in this connection. And as appears by a recent number of Murphy's *Clinics*, Murphy himself adheres to the longitudinal incision which divides the motor nerves of the rectus muscle. Murphy pays particular attention in this supplementary chapter to the end-results of operations on the appendix, to the complications of appendicitis, and to intussusception, tuberculosis, actinomycosis, and malignant tumors of the appendix.

Dr. Hugh H. Young, in revising his chapter on the surgery of the prostate, lays special stress on the beneficial effects of preparatory treatment in reducing the postoperative mortality from renal complications, and claims unequalled value for the phenol-sulphonephthalein test. It is noticeable, also, that he speaks with less contempt than formerly of the suprapubic operation.

Military and naval surgery are ably discussed by Borden and by Bell respectively. Both dwell on the education which is necessary before the average surgeon in civil life can be developed into a medical officer sufficiently competent to take charge of military or naval affairs, or public hygiene; and Borden especially points out the many and increasing advantages, scientific and material, which are open to a young physician who elects to adopt a military career.

New topics of absorbing interest, arthroplasty and transplantation of bone, are ably discussed by Warbasse; while Bickham, in his supplementary chapter on amputations gives admirable descriptions of methods of amputation for cinematic prosthesis. Unfortunately neither he nor Warbasse appear to speak from personal experience.

The volume closes with supplementary chapters on Plastic Surgery, by John B. Roberts; the Surgery of Accidents, by W. L. Estes; Surgery of the Infectious Diseases, by G. E. Armstrong; the X-rays in Surgery, by Codman; and includes moreover a discussion of various modern developments of the anesthetic problem, such as Anesthesia in differential pressure chambers, by Willy

Meyer; Anesthesia by Intratracheal Insufflation, by S. J. Meltzer; Intravenous Ether Anesthesia, by Kummel; and Spinal Anesthesia, by Houghton.

A complete index to the entire series of six volumes concludes this valuable and well nigh indispensable work. A. P. C. A.

TEXT-BOOK OF OPHTHALMOLOGY IN THE FORM OF CLINICAL LECTURES. By DR. PAUL ROEMER, Professor of Ophthalmology at Greifswald; Translated by Dr. Matthias Lanckton Foster, Member of the American Ophthalmological Society, etc. Volume II, pp. 294, 186 illustrations and 13 colored plates; Volume III, pp. 323, 186 illustrations and 13 colored plates. New York: Rebman Company.

THESE are the concluding volumes of this text book of ophthalmology. Volume II contains the chapters upon diseases of the lids, vitreous, sclera, lacrymal organs, and orbit, with chapters upon injuries, glaucoma, and concomitant strabismus. In volume III the affections of the chorioid, retina, and optic nerves, with chapters upon the pupil, pareses of ocular muscles, neurology and functional testing are taken up. An appendix by the translator with a complete index and list of authors concludes the work.

Common sense views pervade the whole. No fads are exploited. The semeiology is presented largely in the form of clinical histories.

As examples of the author's treatment of certain interesting portions of ophthalmology we may select the following as illustrations. Diseases of the orbit are very fully described; the various forms of orbital cellulitis are well set forth, particularly the part played in the etiology and symptoms by disease of the accessory sinuses of the nose. The differential diagnosis from affections of each of these sinuses is well presented. They are held to be responsible for more than 60 per cent. of all cases of inflammatory exophthalmos, hence the invariable rule to examine the accessory sinuses in every case of disease in the orbit—a rule which will lead to the saving of many eyes and the preservation of many lives. But while the nasal origin is thus fully insisted upon, the author takes the ground properly, that the treatment of the underlying sinusitis should be left to the rhinologist, though orbital abscesses must be freely evacuated in the interest of sight as well as of life. Extirpation of the lacrymal sac is declared to be the treatment of chronic catarrhal dacryocystitis. Probing is condemned; Toti's operation is not mentioned. The diseases of the lacrymal passages, epiphora, stricture, acute, and chronic inflammations of the sac are regarded only as individual links in a chain of diseases in which

the general practitioner by proper and timely treatment can take an active part.

Of sympathetic ophthalmia, which is still an interesting and important mystery in ocular pathology, an excellent summary of the views held by leading experimenters is given. There are (1) the migration hypothesis of Leber and Deutschmann; (2) the modified cilioneural hypothesis of Schmidt-Rimpler, and (3) the metastasis view of Berlin and the author. The first assumes the migration of a virulent agent, staphylococcus or other, from the first to the second eye by way of the optic nerve—a view which does not appear consistent with all the phenomena of the disease. Schmidt-Rimpler's hypothesis that irritation of the ciliary nerves in the eye first affected induces a susceptibility in the other through a reflex disturbance, is likewise rejected. Panas' addition to this obscure conception that general toxic influences, such as alcoholism, catarrhal disease of the nose and throat, etc., are predisposing factors, is not regarded as adding strength to the hypothesis. From all the known facts, the author concludes that the only hypothesis yet presented which is also consistent with experiment, is that sympathetic irido-cyclitis originates hematogenously just the same as spontaneous irido-cyclitis, and is due to a specific metastasis from the eye first diseased by an agent yet unknown, which is dangerous to the eye only and not to the other organs. It is obvious that prophylactic treatment will be largely influenced by the surgeon's view as to the pathogeny of the affection.

After detailing the changes usually found in persistent glaucoma and tracing the clinical symptoms to the hypertension, the statement is made that the origin of the latter has not yet been explained, although gain is derived from the knowledge acquired in regard to treatment. Of the three cardinal symptoms in the glaucomatous eye, the changes in the bloodvessels, the cupping of the disk, and the alterations in the filtration angle, the latter alone is amenable to treatment, in that miotics or operations shall free this angle. Of iridectomy the author believes that he states the conviction of soberly thinking ophthalmologists, that while the operation delays the glaucomatous process, it does not permanently cure it; indeed, he advises that miotics should always be tried first whatever the form of disease present. The newer operations such as cyclodialysis and sclerectomy are fairly presented. The origin and outlet of the intra-ocular fluids with the effect of the same and other influences upon the intra-ocular tension are quite fully considered as bearing upon the pathology of glaucoma.

The chapter upon the neurology of the eye gives a good *resume* of the value of ocular symptoms in the diagnosis and localization of disease of the nervous system—so important in certain conditions and valueless in others.

In an appendix, the translator, Dr. Foster, gives an account of

asthenopia, particularly as developed in this country and some of the special methods of measuring the refraction, and also the imbalance of the extrinsic muscles, with some hints as to the appropriate treatment. Asthenopia of nervous origin and the form dependent upon reflex causes are briefly considered.

The work as a whole may be described as a satisfactory exposition of modern ophthalmology. It is perhaps not so well adapted for beginners as certain more elementary text-books and contains nothing strikingly novel; it sets forth modern conceptions clearly for the reader who comes prepared with some previous acquaintance with the subject.

We take pleasure in repeating here what we have said in our review of the first volume, viz., that Dr. Foster has been most successful in giving the work an English dress. It reads almost as if it had been originally written in English and this is high praise for any translation. He is also to be congratulated in having permitted the original German author to expound his own views without doing them to death by constant interpolation of the translator. The book is an expensive one, and this counts in these days when almost every teacher in every medical school, the world over, considers it his bounden duty to put forth in some form, an exposition of his own upon the subject in which he is interested.

T. B. S.

GUIDE TO MIDWIFERY. By DAVID BERRY HART, M.D., F.R.C.P.E.,
Lecturer on Midwifery, School of the Royal Colleges, Edinburgh.
Pp. 765, with 4 illustrations in color and 268 diagrams. New
York: Rebman Company.

HART presents his *Guide to Midwifery* in two parts. The first and larger section is devoted to a clear and full exposition of the necessary facts of obstetrics from a modern standpoint. To each chapter is appended a scheme for the practical instruction of the student. References are made to the various atlases, models or specimens to be examined in connection with the text. References are also given to corresponding sections of the second part.

The author states in the preface his belief that a text-book on midwifery should not be copiously illustrated, but that one should obtain his ideas of the subject from the knowledge gained by the actual handling of specimens. The illustrations are with a few exceptions, well executed and include several excellent colored plates. Many reproductions of frozen sections are shown to illustrate the steps in the mechanism of labor, and the pathological conditions of the parturient canal.

While giving an otherwise good system for the examination and

care of the pregnant woman, in the chapter on hygiene of pregnancy, no mention is made of antepartum pelvimetry or of routine estimation of the blood pressure.

A thorough discussion of eclampsia is given at the expense of only brief notes on the less severe forms of the toxemias of pregnancy. The repeated statement that chloroform may be given with entire safety to the pregnant woman, especially in the treatment of eclampsia, may be subject to question in the light of recent investigations.

Proper emphasis is placed on the importance of breast feeding in a well written section on the infant. Among the pathological conditions of the infant no mention is made of hemorrhagic disease or of its successful serum therapy.

The various obstetrical operations are described in detail. The classical Cesarean section being favored by the author in the treatment of labor in contracted pelvis rather than the girdle splitting operations or the lately revived extraperitoneal Cesarean section.

The second part of the book entitled "Notes and Discussions" takes up in an order corresponding to the first part the various theories, old and modern concerning disputed points. New operations are described and comparative statistics are included. In the chapter on evolution of obstetrics is found a discussion of Darwinism, Mendelism, and Weissmanism and their relation to this branch of medicine. A short section sums up the more recent views of the relations of the organs of internal secretion to the reproductive period.

The literature is given in a separate section under specific headings and a comprehensive index is added. There is much to be recommended in the book, especially the method of arrangement.

P. F. W.

THE SURGERY OF THE STOMACH. A HANDBOOK OF DIAGNOSIS AND TREATMENT. By HERBERT J. PATERSON. Pp. 304; 74 illustrations. New York: William Wood & Company, 1913.

WE have in this volume a consideration of a field of surgery which, in its scope and usefulness, is growing rapidly. It is covered fully but not with burdensome detail. The methods of examination and the operations described, and the opinions expressed, are almost entirely those employed by the writer. Little space is given to the work of others in this field, except to that of W. J. Mayo who is freely quoted and to whom the book is dedicated. The first chapter of sixteen pages is devoted to the method of investigating gastric conditions, including those of the duodenum, and at the

end of the book is an appendix of fifteen pages in which is described the technique of the various methods of examining the gastric contents. The descriptions of operations and the illustrations are, in the main, excellent, although some of the views expressed are not in agreement with those commonly entertained. For instance, it is not generally agreed that it is immaterial whether the anterior or posterior gastrojejunostomy be performed. Nor is it in accord with general surgical practice in this country to sacrifice the advantages of the Roosevelt or other three-jawed clamps in this operation. The description of gastrectomy is somewhat confused by the fact that the illustrations are those of W. J. Mayo, and the writer's description does not tally with them, particularly with regard to the application of the clamps. Nor does it seem proper to approve in a book of this kind, the recommendation of proprietary articles of food, one of which has been especially offensive in its method of advertising, and has been criticised by our representative medical journals. These, however, are minor deficiencies and do not retract from the generally high standard of the work, which will undoubtedly meet with an appreciative reception from those who need books of this kind. At the end of each of the more important chapters is a valuable summary of the important facts in the chapter, which will aid the reader in carrying the facts to the bedside and operating table.

T. T. T.

HYPNOSIS AND SUGGESTION. By W. HILGER, M.D., of Magdeburg, Translated by R. W. FELKIN, M.D., F.R.S.E. Pp. 233. New York: Rebman Company.

THE introduction to this book is a practical summary of what follows, it being written by Dr. Van Renterghem. Judging from it and from the contents of the volume itself, it is principally a defense and exposition of the fact that Liebeault of the University of Nancey was the originator of modern hypnotism and its treatment. It then gives a history of this master, his methods and the theories upon which hypnotism are based. According to him healthy persons are most suitable for hypnotic treatment, whereas Charcot and those who followed him claim that hypnosis could be induced only in those suffering from nervousness, especially hysteria, and that it was a dangerous weapon, useless for therapeutics and only useful for experimental research. Following Liebeault, Bernheim, Vogt, and Forel did excellent work in hypnosis. There is a scathing criticism of Dejerine and Dubois, in which the former is accused of having made use of the writings of Liebeault without giving him credit, while of the latter, who

published his book in 1904, it is said that in reading this book everything that is worth while in suggestive therapeutics originated with him. On the contrary, great credit is given the new school of psycho-analysis as exemplified by its originator Breuer and its most famous exponent, Freud.

The volume itself, while it is written for the laymen and the general practitioner, is nevertheless a very good exposition of hypnotism, its methods of application and the results to be obtained from it. Everyone of us know that there is a deep-rooted skepticism of the uses of hypnosis in the treatment of disease. This is largely because of the commercial uses made of it. That hypnotism is a legitimate and excellent method of treatment for some functional diseases, there is no question, for certainly such men as Vogt, Forel, and others who have been mentioned would not use it. The truth of the matter is that hypnotism should be employed, but carefully, and *only* in the hands of those who are thoroughly capable of applying it. Its indiscriminate use by poorly trained individuals should be strongly condemned. The author has apparently had good results, but even he makes claims which are somewhat difficult to believe.

T. H. W.

THE CARE OF THE SKIN IN HEALTH. By W. ALLAN JAMIESON, M.D., Consulting Physicians for Diseases of the Skin, Edinburgh Royal Infirmary. Pp. 109; 2 illustrations. London: Henry Freude, Hedder and Stoughton.

THE author divides the subject matter in his little volume into an easily understood description of the structure of the skin, the care of the skin, the care of the hair and the nails, and suggestions as to diet and clothing. The small work is evidently intended for the general public as the author has made the entire volume quite understandable to the lay comprehension. Particular stress is laid upon the bathing regulations, as to the temperature of the water, the composition of the soap, and frictional exercises following the ablution.

F. C. K.

MANISCH-DEPRESSIVES UND PERIODISCHES IRRESEIN ALS ERSCHEINUNGSFORM DER KATATONIE. Eine Monograph von DR. MED. MAURICY URSTEIN, Warschau. Pp. 650. Berlin und Wien: Urban und Schwarzenberg, and Rebman Co., N. Y.

THIS monograph is the complement of the previous one written by the author upon *Dementia Præcox and its Relation to Manic-*

depressive Insanity. The present work is upon manic depressive and periodic insanity, and its relation to katatonia. The author comes to the conclusion that these two types of insanity should not be considered as distinct, but are really states of katatonia. He bases his conclusion upon an analytical study of thirty cases. It is a splendid bit of work, and should be read by everyone who is interested in insanity because it exemplifies what can be accomplished by profound analytical study, and is a distinct advance in modern psychiatry.

T. H. W.

GOULSTONIAN LECTURES, 1912; MODERN VIEWS UPON THE SIGNIFICANCE OF SKIN ERUPTIONS. By H. G. ADAMSON, M.D., F.R.C.P. (Lond.), Physicians for Diseases of the Skin, St. Bartholomew's Hospital. Pp. 103; 43 illustrations. London: John Bale, Sons & Danielsson.

ALTHOUGH practically every other field of medicine has been covered in the Goulstonian lectures, a dermatologist has not delivered this series of talks since Dr. Liveing delivered his classical exposition upon leprosy. The little volume under review consists of the three lectures delivered by Dr. Adamson before this representative body. No more interesting subject could have been selected than the study of the significance of skin eruptions, as viewed from the most modern and advanced point of view. A considerable portion of the volume is devoted to local and general immunity in various diseases of the skin and to the interesting subject of anaphylaxis. The local reaction of the different layers of the skin, depending upon the irritating stimulus is plainly shown. The author takes the view, that in at least certain diseases, the eruption is a defensive reaction to the causative reagent; the type of the outbreak depending upon the character of the stimulus. The very interesting local and general immunity that is produced in certain deep-seated trichophyton and the cuti-reaction to cultures of the ringworm are among the most interesting details presented in the book. Among other phases of the subject touched upon are the relationship of immunity production to the treatment of skin diseases; the idea and the origin of toxins; the relationship of toxic bodies to erythematous, urticarial, and drug eruptions; the origin of eruptions resulting from toxins from a distant bacterial focus; auto-intoxication; the significance of the patterns and distribution of skin eruptions, as to the influence of local physical agents. The little volume cannot be too strongly recommended to all those interested in dermatology and modern views on the etiology of diseases of the skin.

F. C. K.

MINOR SURGERY. By LEONARD A. BIDWELL, F.R.C.S., Senior Surgeon to West London Hospital, Dean of Post Graduate College, etc. Second edition; pp. 292; 129 illustrations. London: University Press, by Hodder & Stoughton, and Henry Froude.

THIS work has gone to its second edition in twelve months, an argument in favor of its meeting the needs of the times. In every respect the changes in this edition are improvements over the first edition. The size of the volume, the binding, and the more extensive index are all advances. There has been added a chapter on bandaging and minor injuries which contain all that is necessary for a general practitioner to know. The work is not meant to be a completed treatise on any one of its subjects, but is meant to give simple and clear directions for the management of everyday surgical procedures. The attention to detail is worthy of note everywhere in the book with but few exceptions, and in many instances the author states facts of utmost importance, which have been experienced by him and yet are not mentioned in more extensive works in surgery.

The text is clear, concise, and to the point. There is no theorizing and no statements made that are not proved facts. Symptomatology is not touched upon, the entire work being given to treatment. The book is an admirable one for students, nurses, internes, and general practitioners, but is rather too elementary for surgeons of any experience, which I believe is the claim made by the author.

E. L. E.

STUDIES IN PSYCHIATRY. By MEMBERS OF THE NEW YORK PSYCHIATRICAL SOCIETY. Pp. 222; 14 illustrations. New York: The Journal of Nervous and Mental Disease Publishing Co.

As represented by the title this volume consists of reprints of fifteen papers written by various members of the New York Psychiatric Society. It is difficult to pick out a particular paper of this important group for review. Perhaps the most interesting is one by Dr. Frederick Peterson on "The Insane in Japan," and one on "The Curability of Early Paresis," by Dr. Charles L. Dana.

The papers here represented constitute the first of a series which are to be published by this Society.

T. H. W.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Primary Splenomegaly (Gaucher Type).—MANDELBAUM (*Jour. Exper. Med.*, New York, 1912, xvi, 797), after a review of the reported cases and study of a case of his own with autopsy, concludes that primary splenomegaly of the Gaucher type is a distinct disease, related in all probability to the blood diseases. It begins usually at an early age, frequently affects several members of a family, and runs a chronic course. The clinical manifestations are: Pronounced hypertrophy of the spleen; subsequent enlargement of the liver; discoloration or pigmentation of the skin; tendency to epistaxis or other hemorrhages; absence of palpable lymph nodes; absence of jaundice and ascites, and absence of characteristic blood changes. The lesions are found in the spleen, lymph nodes, bone marrow, and liver. These organs show iron-containing pigment and large multinuclear cells with a characteristic cytoplasm. In the early cases, peculiar large phagocytic cells arising from atypical large lymphocytes are found in the follicles of the hemapoietic system. After leaving the follicles these cells possess phagocytic qualities for a certain period. As a result of the phagocytosis the cells enlarge, the nature of the cytoplasm changes, and the cells acquire a characteristic vacuolated and wrinkled appearance. The cells are carried from the spleen through the portal system to the liver, where they are destroyed. The irritation produced by this destructive process gives rise to an increase in the intralobular connective tissue. The disease is eminently a chronic one, without any of the manifestations of malignancy, and always terminating as the result of some intercurrent affection. The etiology is unknown, although a family predisposition to some toxic agent which causes an

irritability of the follicles in the hemapoietic system probably exists. The possibility of some protozoan infection, as an etiological factor, must not be overlooked.

Renal Diabetes during Pregnancy.—J. NOVAK, O. PORGES, and R. STRISOWER (*Deutsch. med. Woch.*, 1912, xxxviii, 1868) have made a study of the spontaneous glycosuria of pregnancy. In 2 cases they found that the excretion of sugar was independent of the diet. With the carbohydrates eliminated from the food, sugar was still excreted in the urine; but an abundant supply of carbohydrates in the diet did not lead to a corresponding increase of the sugar in the urine. Furthermore, they found that the glucose content of the blood was normal, even subnormal. They were dealing, therefore, with a condition which has been described as renal diabetes, in which it is supposed that the kidney, as in phloridzin glycosuria, is abnormally permeable to sugar. The previously recorded cases have been unassociated with pregnancy. It was anticipated by the authors, then, that the occurrence of renal diabetes in 2 consecutive pregnant women was more than a coincidence. They have been able to observe 5 other pregnancies with glycosuria, and in none of them was there a hyperglycemia, in none was the quantity of glucose in the urine influenced to any considerable degree by variations in the quantity of carbohydrate consumed. In 2 of the patients who have been delivered, the glycosuria has ceased spontaneously. Novak, Porges, and Strisower are of the opinion that renal diabetes and pregnancy are not infrequently associated.

Edema of the Lower Part of the Esophagus from Vomiting.—At the suggestion of Professor Schmorl, F. ROST (*Deutsch. med. Woch.*, 1912, xxxviii, 1694) has examined the esophagus in a large series of autopsies. This was done, because Schmorl had noticed a rather marked edema of the cardiac end of the esophagus in several cases of septic peritonitis. Rost's study showed that edema is the rule in such cases. It affects the mucosa, the submucosa, and extends into the muscularis mucosæ. The edema seldom extends more than 3 to 5 cm. above the cardiac end of the esophagus; in other words, it affects the intra-abdominal portion of the esophagus. In all cases where marked edema was found, vomiting had been a prominent symptom. In other conditions with frequent vomiting shortly before death, such as strangulation of the bowel, cancer of the stomach, etc., edema was found only in about one-half of the cases; it was never very marked. Again, in cases of septic peritonitis in which there had been little vomiting, edema was usually slight. The author believes, therefore, that vomiting is an important factor in the production of edema of the lower end of the esophagus, but that the toxins absorbed from a septic exudate also promote its development.

Experimental Observations on the Influence of Venesections and Intraperitoneal Blood Injections on the Number and Resistance of Red Blood Corpuscles.—K. OCZESALSKI and ST. STERLING (*Deutsch. Arch. f. klin. Med.*, 1912, cix, 9) have tested the effect of withdrawal of blood and of intraperitoneal blood injections experimentally on

rabbits, in an attempt to discover whether the method might have value in the treatment of human anemias. They find: (1) Venesections, even when large, if not repeated at too frequent intervals, not only produce no harm, but cause an increase in the resistance of the red blood cells. (2) Venesections in connection with injections of the same blood in the peritoneal cavity are harmless to the healthy animal and increase the resistance of its red blood corpuscles and also the total number of red cells. (3) Venesections in connection with injections of the shed blood in anemic animals cause an increase of hemoglobin and total red count and of the resistance of the red blood corpuscles. A similar procedure would seem to be justifiable in simple, chronic, post-hemorrhagic anemias, of course, with strict asepsis. (4) Injection of foreign blood following venesection produces the same results in anemic animals as described in (3). Clinically, this is less useful, as a donor must be found. (5) The same results follow the injection of foreign blood without venesection.

On the Relation of Eosinophilia to Anaphylaxis.—H. SCHLECHT and G. SCHWENKER (*Deutsch. Arch. f. klin. Med.*, 1912, cviii, 405) summarize their experimental observations on the relation of eosinophilia to anaphylaxis as follows: Through continued parenteral administration of foreign protein a peripheral blood eosinophilia may be produced in the guinea-pig. With large doses a similar result may be obtained in dogs. Following recovery from anaphylactic shock an intense eosinophilia likewise occurs. Furthermore, the lungs of guinea-pigs which have withstood anaphylactic shock, exhibit a marked eosinophilic infiltration of the lung tissue and a peribronchial collection of these cells. Similar changes may be produced in animals sensitized intraperitoneally, by inhalation of serum. The peribronchial and pneumonic infiltrations are markedly eosinophilic, in contrast to the pneumonias produced by inhalations of bacteria. In Arthus' skin phenomenon the cells of the inflammatory swellings are chiefly eosinophiles. A local eosinophilia of the submucosa is seen in the intestine of dogs following anaphylactic enteritis. A local production of eosinophilous was not observed in these conditions. It is evident that the eosinophiles play a definite role in anaphylaxis. The authors are inclined to the view that certain products are formed in parenteral administration of protein which exert a positive chemotactic action upon the eosinophilic cells; they are attracted from the blood and bone-marrow, where they are present in increased numbers. Whether they are dealing with a single substance or several distinct bodies is unknown.

Observations in Two Cases of Pentosuria.—KJ. OTTO AF KLERCKER (*Deutsch. Arch. f. klin. Med.*, 1912, cviii, 277) has made a careful study of the urine of 2 patients with pentosuria. It is of interest that the patients were brothers, that a third brother suffered with diabetes mellitus, and that the father of the three was a diabetic. Klercker found that the osazone obtained from the urine of each patient was dextrorotatory. By the degree of rotation found, it is practically certain that the pentose in one of the cases was l-arabinose, while in the other there was a mixture of the d- and l-components, with the

l- predominating. These findings are in line with those of Neuberg and Luzzatto. It is evident, therefore, that in pentosuria the isomers may be mixed in varying proportions. The source of the pentose remains obscure. The nucleoproteids of the body cannot be excluded. Hunger or insufficient food causes a decrease in the excretion of the pentose. Like other observers, the author has found no relation between the glucose of the food and pentose excretion. The parallelism in the excretion of pentose and total nitrogen determined hourly is striking, and suggests an intimate relationship between the pentose and protein metabolism. Glucosamine, as shown by the results of administering it to the patients, does not increase the amount of pentose in the urine. Klercker was able neither to confirm nor refute Neuberg's observation regarding the possibility of formation of pentose from galactose. Following the administration of lactose, there was a sharp rise in the quantity of pentose in the urine, which did not, however, increase the total output beyond the theoretically possible limit.

On the Production of the so-called "Zellschollen" in Lymphatic Leukemia.—A. SPULER and A. SCHITTENHELM (*Deutsch. Arch. f. klin. Med.*, 1912, cix, 1) report their observations on a case of lymphatic leukemia. The so-called Gumprecht's shells or shadows which one sees in lymphatic leukemia, arise from lymphocytes with relatively pyknotic nuclei through bursting of the nucleus and mixture of the nuclear constituents with those of the cell protoplasm. The study of a fresh gland from a patient revealed similar pyknotic cells. From this material it was evident that the chromatin of the cells in addition to being diffusely distributed is also seen in clumps or plump strands. Germinal centres, such as are found in the normal lymphatic glands, were not encountered, but areas in which mitoses were numerous indicated that there was active proliferation of the cells. Phagocytosis of red blood cells was observed in the lymphatic glands. A gradual transition of these phagocytes to typical eosinophiles, whose nuclei later became polymorphous, was observed. These cells originated locally and not from bone-marrow elements.

Disturbances in the Hydrochloric Secretion in Diseases of, and following Extirpation of the Gall-bladder.—H. HOHLWEG (*Deutsch. f. klin. Med.*, 1912, cviii, 255) reports gastric analyses from a large number of patients with disease of, or following extirpation of the gall-bladder. He found after extirpation of the gall-bladder that of 39 patients only 10 per cent. had normal hydrochloric acid following a test breakfast. The remainder (74.3 per cent.) had either sub-normal values or an actual deficit of hydrochloric acid. Three cases with normal acid were not included in the series; two suffered from gastric ulcer, the third had icterus, conditions frequently associated with hyperacidity. Hohlweg believes that a more careful analysis would have resulted in the diagnosis of similar complications in some of the other cases with normal hydrochloric acid. Among 43 patients with closure of the cystic duct or atrophy of the gall-bladder, 84 per cent. exhibited a hydrochloric acid deficit, 6 patients had subacidity, and only once was the hydrochloric acid normal in quantity. The

conditions here are, therefore, analogous to those following extirpation of the gall-bladder, and the gastric findings are the same. In a series of 15 cases of cholecystitis, some with calculi but without closure of the cystic duct, hydrochloric acid deficit was found 13 times, and in the remainder there was subacidity. Hohlweg next examined the gastric contents of dogs before and after cholecystectomy, and the results were similar to those encountered in man. In a young married woman the gastric contents during an attack of gallstone colic showed a hydrochloric acid deficit of 20, total acidity of 32. Two stones were recovered from the stools. A week later free hydrochloric acid 38, total acidity 74. Finally, Hohlweg cites several histories of elderly patients with loss of weight, gastric symptoms, and hydrochloric acid deficit, in whom a diagnosis of gastric cancer was made. Operation showed nothing in the stomach, but there was marked disease of the gall-bladder.

Calcium Metastases and Calcium Gout.—M. B. SCHMIDT (*Deutsch. med. Woch.*, 1913, xxxix, 59) has made a careful study of a case presenting extensive calcification and has arrived at the following conclusions: An excess of calcium in the blood alone can lead to deposition of calcium in healthy organs, as shown in Tanaka's experiments and in many cases of calcium metastases in skeletal diseases of man without nephritis. This, however, is uncommon in man, for usually there exists a nephritis. On the other hand, extensive calcification may occur in some parts of the body, without increase of the calcium contained in the blood, through resorption from the bone; in such cases there is usually, but not always, a nephritis. In these cases the author believes that there is not a primary dystrophy but rather an altered (lowered) solubility of calcium in the blood. The usual participation of the acid-secreting organs in the calcification can occasionally be augmented by pathological changes in the tissues. In the pathologically predisposed organs—lungs, gastric mucosa, kidneys, bloodvessels and possibly the myocardium—calcification, can occur without preceding pathological changes, as happened repeatedly in Schmidt's case. When necrosis is found after dissolving the calcium, Schmidt believes it is to be interpreted as the result of the deposition calcium, not the cause. Such a conception is similar to the prevailing theory regarding gout, namely, that gouty deposits result from a primary disturbance of uric acid metabolism with precipitation of salts in healthy tissues and secondary necrosis. Therefore, the name calcium gout is appropriate for the condition described.

A Method of Differentiating between Ascites and Fluids from Ovarian Cysts.—A. DIENST (*Münch. med. Woch.*, 1912, lix, 2731) alludes to the importance of differentiating at times between ascites and a flaccid ovarian cyst, if exploratory operation is refused and one has to resort to tapping of the abdomen. The appearance of the fluid may not be characteristic, for at times the fluid of the cyst closely resembles the usual serous ascitic fluid and, on the other hand, a pseudochylous or chylous ascitic fluid is not unlike many fluids obtained from cysts. Dienst has found that fibrin is a constant constituent of ascitic fluids, while it is absent in the fluids of ovarian cysts. As a

qualitative test for fibrin, he adds to the fluid in a test-tube crystals of sodium chloride equal to one-third the volume of the fluid. After solution of the salt a flocculent precipitate forms, if fibrin is present. The absence of a precipitate indicates that the fluid was obtained from a cyst and shows the need of operation.

SURGERY

UNDER THE CHARGE OF

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The Radical Operation for Cancer of the Uterus.—CLARK (*Surg., Gynec., and Obst.*, 1913, xvi, 255) offers the following summary from a review of the literature and from personal experience: The operation in expert hands, notwithstanding its high primary mortality, has given the greatest of permanent cures of any therapeutic procedure thus far suggested for cancer of the uterus. While the above conclusion is true, the general adoption of the operation, in view of its dangers and difficulties, is not to be advised until the primary mortality can be reduced to a much lower percentage by simplification or perfection of details. The abandonment of the extensive glandular dissection is justified, because this detail adds to the hazards and does not sufficiently raise the percentage of permanent cures. The cardinal advantage of the operation lies, first and above all, in the excision of an extensive cuff of vagina and the widest possible removal of the parametrial tissue. There is no middle-of-the-road policy in cancer of the cervix. The surgeon would better perform a simple hysterectomy or high amputation of the cervix with extensive cauterization than to attempt the radical operation if he is not prepared effectively to execute its details. The earnest endeavor by many specialists, with the improved ultimate cures in a few hands, offers the hope that a further simplification and perfection of details in this operation may yet make it more generally available.

Results after the Wertheim Operation for Carcinoma of the Cervix of the Uterus.—NEEL (*Surg., Gynec., and Obstet.*, 1913, xvi, 293) made a study of the cases treated at the Johns Hopkins Hospital and concluded that the extensive abdominal removal of all uterine cervical carcinomas is justified where there is any hope of complete excision. An exploratory laparotomy is often necessary to determine whether

or not a case is operable. The preliminary catheterization of the ureters is a valuable aid, especially in fat patients, and does not necessarily increase the probability of fistulæ or secondary infection of the urinary tract. Preliminary cauterization and disinfection of the primary growth is advisable in all cases. A horizontal lipectomy in obese patients decreases the depth of the field of operation and shortens the time necessary for its completion. All patients should be kept in the Fowler position for several days, unless this is otherwise contraindicated by symptoms of surgical shock. By improvements in the technique of the operation, the primary mortality has been decreased from 28.5 per cent. for the first seven years to 11.7 per cent. for the last five years. Aside from the discovery of the etiological factor of carcinoma of the cervix of the uterus and its successful elimination, the greatest hope lies in the early recognition and wide excision of the primary growth.

The Treatment of Beginning Gangrene.—BORCHARDT (*Zentralbl. f. Chir.*, 1913, xl, 297) says that the question of when and where to amputate for gangrene of the foot is still undecided. Moskowicz decided the site by observing the level to which the reactive hyperemia of the skin reached, after a temporary removal of the blood from the affected limb. In this way he determined how much of the tissues were being supplied with blood. Borchardt regards this as a good aid in determining to what extent the tissues are being nourished, but says that the temporary application of a tourniquet is exceedingly painful to some patients, and that in cases with severe arteriosclerosis the necessary evacuation of blood and reactionary hyperemia cannot be obtained. Its application has little influence in improving the condition of the circulation and preventing the gangrene. He employed the following method in a man, aged fifty-four years, with senile gangrene of the toes and severe pain. After three months existence of the gangrene, two toes had been exarticulated, and later, as the gangrene was of the moist variety and there was a phlegmon of the foot, amputation in the thigh was performed. It was observed that at the site of amputation the femoral artery was almost closed. After a very severe struggle he recovered. Then there began in the other foot symptoms of beginning gangrene, just as in the first foot, with severe pain, cyanosis, etc. As the usual treatment, including elevation and moist warmth, failed, Borchardt concluded to employ alternating warm and cold baths of the limb to the knee. Two deep buckets were filled with water, one at a temperature of 35° C., the other with standing water. The limb was placed in each bucket alternately, for a few seconds. The changing from one to the other was repeated in the beginning thirty times, later fifty times. Gradually the temperature of the water was increased to 50° C. in the one bucket, and in the other to that of running water. These baths were taken morning and evening for a week, when the pain promptly disappeared. During the baths the leg was always very red and warm. It showed a more active hyperemia than with the use of the warm water alone. The patient has continued the baths for three-fourths of a year, and has not developed gangrene in this limb. On the contrary, the circulation of the limb shows continuous improvement. The baths stimulate the

collateral circulation and can considerably improve the peripheral blood supply in the presence of existing gangrene, and thus extend, peripherally, the limit of the amputation area. The method should not displace the present methods, as Moscowicz's method, but should amplify them.

The Diagnosis and Treatment of Gangrene of the Foot.—Moscowicz (*Zentralbl. f. Chir.*, 1913, xl, 507) calls attention to the fact that the objections to his method raised by Borchardt, can be overcome. He has often found that the application of the tourniquet is unnecessary. It suffices in most cases to elevate the affected limb for one or two minutes, in order to render it bloodless. That alone is a sign of disturbed circulation, since a mere elevation should not produce such a complete anemia. If the limb is then let down it slowly becomes red, but much more slowly than if the arteries are normal. In many cases he has allowed the limb to hang down vertically to favor the return of the blood, and even in this position one or several toes have remained pale a long time or persistently. By thus changing the position of the limb the same changes in circulation can be obtained as by Borchardt's alternating baths. He has also seen in one patient the pain of a deficient circulation moderated by the use of Klapp's suction apparatus, and the beginning gangrene probably retarded. He does not doubt that Bier's method of inducing passive hyperemia has a similar effect in quieting the pain and improving the nourishment. It is probable that the anastomosis of the femoral artery and vein will produce a similar effect, the more through the stasis due to the ligation of the vein than to the turning of the blood stream.

The Treatment of Beginning Gangrene.—FRANK (*Zentralbl. f. Chir.*, 1913, xl, 508) confirms the value of Borchardt's method with the report of a striking case. A soldier suffered from frozen feet, which, on both sides, including the lower thirds of the legs, were edematous, cyanotic, cold, and tender on the dorsum of the feet. From the tender areas downward, they were without feeling. There was severe, almost unbearable pain in the parts of the limbs involved which had feeling. The saving of the toes and middle portions of the feet seemed hardly possible. It seemed that a Chopart amputation would be necessary. At best a Lisfranc, and at the worst an amputation in the upper third of the leg was in prospect. The alternating baths were tried and kept up for six months. The effect was striking. The right foot is now sound and useful. On the left side the great toe and a part of the plantar fascia were excised for gangrene. All the other tissues were preserved.

The Treatment of the Pyelotomy Wound.—BASTIANELLI (*Zentralbl. f. Chir.*, 1913, xl, 420) says that surgeons are now favoring pyelotomy for renal calculi as against nephrolithotomy, but that the special technique has not yet received much attention. He believes that if the proper indications are observed and the operation properly performed, the details of the suture are not particularly important. The wound in the pelvis heals without suture, if there is no obstruction

to the outflow of the urine, the infection is not severe, or the wound is not too large or irregular. Yet it is not advised that the suture should be systematically avoided. The incision may be made directly through the fat and pelvic wall, and the closure made by catgut sutures which include both layers to the submucosa. This applies especially to cases in which the kidney cannot be delivered from the wound. In one case a large calculus was exposed through a pelvic incision. Because the stone could not be palpated easily, the pelvis was well freed from the surrounding fat. After extraction of the stone, the sutures used to close the pelvic opening cut through. The wound was not superficial and its closure was accomplished by a quadrilateral flap taken from the fibrous capsule of the kidney, from which the fat was removed. Mayo used the fatty capsule for a similar purpose. In cases with stones in the calyces, the pelvis should not be explored too much with the finger or forceps, but a radial incision should be made directly over the stone through the renal parenchyma. The wound can be closed with sutures, and these overlaid with a fatty flap with good results. In a mildly infected hydronephrosis, the cause of which was a stricture at the upper end of the ureter, the pelvis was widely opened, the stricture divided anteriorly, and posteriorly. The wound was then closed in a transverse direction with a single row of sutures, and covered with a broad, fatty flap. Primary union resulted. When, because of the depth of the wound and the shortness of the pedicle, the kidney cannot be delivered, the fat should not be freed from the pelvis, but the incision should be made directly on the stone and the wound afterward left unsutured. The surrounding fatty tissue applies itself over the wound and closes it.

The Etiology, Symptomatology, and Pathogenesis of Acute Intestinal Obstruction.—POLACCO and NEUMANN (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxii, 42), in an operation for an acute intestinal obstruction, found the jejunum, at about its middle, strangulated by a long, thin, fibrous band, which passed from one coil of intestine to another. In this central portion of the jejunum were a number of protuberances from the surface of the bowel, each about the size of a pea and rather firm in consistency. The strangulated portion of the jejunum was encircled by a ring formed by the fibrous band which seemed to be formed by the union end-to-end of two elongated and pedunculated protuberances, similar to those found on other portions of the bowel. After the division of the band, the serosa at the site of strangulation was seen to be smooth, and the distal coils of intestine immediately filled with gas. The numerous, peculiar protuberances which were most numerous in the direction of the appendix suggested that a previous appendicitis combined with a fibrous peritonitis may have been responsible for them. The appendix was found posteriorly, surrounded by fibrous adhesions which showed the same peculiar protuberances found on the intestine. The appendix was removed as well as some of the protuberances. The histological examination disclosed that the rounded ends of the protuberances were made up of a connective tissue, rich in nuclei, and had a similar connective tissue capsule. There was some necrosis, partial hyaline degeneration, and edematous infiltration. The pedicle possessed abundant young

connective tissue and capillaries. It is concluded that there occurs an apparently little-known development of organized peritoneal exudate, in the form of a pedunculated formation, the end being about the size of a pea. Two such bodies may adhere to each other and cause a probably post-traumatic (as from blows on the abdomen) strangulation of the intestine. In these cases two rare symptoms occur; a bradycardia with a pulse of about 52, and a retardation of the effect of morphine. The latter is probably due to the administration of the morphine by mouth into a well-filled stomach. A quick and easy cure can be obtained by a right-sided operation.

THERAPEUTICS

UNDER THE CHARGE OF

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Whooping Cough. Its Treatment with Vaccine.—WILSON (*New York Med. Jour.*, 1913, xcvi, 823) reports a series of 24 children with whooping cough treated by pertussis vaccine. He gave the vaccine in doses of 20,000,000 to 40,000,000 bacteria. The dosage was controlled, after the initial dose, by the range of temperature and the severity of the cough. The paroxysms diminished in frequency and in severity and in some of the children very promptly. The characteristic whoop disappeared and the cases soon became clinically simple cases of bronchitis. The shortest duration of treatment was nine days, the longest forty-eight days, and the average twenty-three days.

The Vaccine Treatment of Whooping Cough.—SILL (*Amer. Jour. Dis. of Child.*, 1913, v, 379) has employed pertussis vaccine for the treatment of 33 children suffering from whooping cough. He believes that the vaccine markedly diminished the number and severity of the paroxysms and the amount of vomiting. The dosage of the vaccine was regulated more by the severity of the disease than by the age of the child. The youngest child treated was one month old and the oldest was six years. Most of the children were from six months to three years of age. The dosage of the vaccine varied from 20,000,000 in the mild cases to 60,000,000 in the severe cases. The cases that were treated early in the disease seemed to respond more quickly to the treatment, and the course of the disease was shortened. In all cases, however, after one to three injections the number and severity of the attacks were markedly diminished. The children showed greater improvement when the vaccine was given in moderately large doses at intervals of from one to two days. Sill advises as the correct dosage for mild cases 50,000,000 bacteria every other day, and for severe cases this same dose every day or 100,000,000 every other

day. The vaccine is given subcutaneously in the abdomen or buttocks, and no untoward effects were noted. No inflammation, swelling, or constitutional symptoms occurred after the injections. Sill also gave the vaccine to children constantly exposed to whooping cough, as a prophylactic measure, and none of these children contracted the disease. He believes that the vaccine when injected in small doses has a certain immunizing action against whooping cough.

The Effect on the Nervous System of Healthy Rabbits of Large Doses of Salvarsan.—DOINIKOW (*Munch. med. Woch.*, 1913, lx, 796) writes concerning experiments undertaken to determine whether the hemorrhagic encephalitis reported by many different observers as a result of salvarsan injections was really due to salvarsan. He could determine no histological changes in the nervous system of rabbits that received for long continued periods of time considerably larger doses than the usual therapeutic doses of salvarsan. Only in experiments where distinctly poisonous doses were used (0.11 to 0.15 gram per kilo) could any alterations in the nervous systems be determined. These alterations consisted of congestion and hemorrhages, but no thromboses of the cerebral vessels were found.

Neosalvarsan.—DREYFUS (*Munch. med. Woch.*, 1913, lx, 630) says that neosalvarsan seems in general to be milder and less intensive in its action than salvarsan, therefore salvarsan is to be preferred in the treatment of syphilitic diseases of the central nervous system. Dreyfus thinks that the combined use of salvarsan and neosalvarsan may be of great value in the treatment of many cases of syphilis. One must not forget that untoward by-effects occur with the use of neosalvarsan in spite of its greater solubility. He emphasizes the importance of using freshly distilled water and that the water should be distilled and the solutions made in Jena glass. This last precaution is necessary because certain by-effects observed after intravenous injections of salvarsan have been attributed to the action of alkali from glass.

Mercury and Salvarsan.—FINGER (*Wien. klin. Woch.*, 1913, xxvi, 561) says that salvarsan should be used in combination with mercury in early syphilis as a means of abortive treatment. He also advises the use of salvarsan in tertiary syphilis when a rapid effect is desired. Finger, however, believes that salvarsan is not superior to mercury in secondary syphilis, and, furthermore, it should not be used as a routine measure in the treatment of secondary syphilis because of certain dangers. He refers especially to the cranial nerve symptoms that have seemed to occur so much more frequently since the use of salvarsan and that have been directly attributed by some observers to the salvarsan injections.

Trivalin.—MEHLISS (*Deutsch. med. Woch.*, 1913, xxxix, 65) says that trivalin is an efficient substitute for morphine in any case where the anodyne or sedative action of morphine is desired. Trivalin has no untoward action on the heart, respirations, or sensorium of the patient, and is, furthermore, less apt to cause gastric disturbance. Trivalin is a combination of morphine, caffeine, and cocaine valerianate.

Adigan, a New Digitalis Preparation.—FRÄNKEL and KIRSCHBAUM (*Wien. klin. Woch.*, 1913, xxvi, 605) write concerning adigan, which is a preparation derived from digitalis. This remedy contains all of the active principles of digitalis with the exception of digitonin and similar saponin-like substances, that have been removed. They claim that the preparation, because of this purification, is free from untoward by-effects especially those of gastro-intestinal irritation and according to their clinical observations the remedy has lost none of the therapeutic effects of digitalis.

The Value of the Karell Diet.—WITTICH (*Deutsch. Arch. f. klin. Med.*, 1913, cx, 128) gives his findings regarding the worth of the Karell diet based upon 100 cases of different forms of heart disease. He believes that it causes a marked improvement in practically all forms of cardiac disease and considers that the only contraindication to its use is the presence of uremic symptoms. Chronic myocarditis seems to be more favorably influenced than any other form of cardiac disease. Valvular lesions of the heart are next in order as regards benefit obtained from the Karell diet. Symptoms of cardiac failure in chronic myocarditis are relieved by the dietetic treatment alone, but in valvular disease it is often necessary to combine cardiac tonics with the Karell method of diet. Cases of cardiac failure due to arteriosclerosis are less favorably influenced, and those associated with nephritis are often very little benefited by the Karell diet. However, in some cases of nephritis the diet is of great value in conjunction with medical treatment. When uremic symptoms are present abundant fluids are indicated, and this necessitates a modification in the Karell diet the principles of which are a low chloride content and a limited amount of fluid.

The Treatment of Vincent's Angina.—CITRON (*Berl. klin. Woch.*, 1913, l, 627) describes two cases of Vincent's angina that were cured promptly by the local application of a 2 per cent. solution of salvarsan in glycerin. The intravenous use of salvarsan in one of these cases was entirely without effect.

The Treatment of Local Spirochete Infections by Salvarsan and Neosalvarsan.—GERBER (*Münch. med. Woch.*, 1913, lx, 634) advises the use of salvarsan and neosalvarsan in local infections due to spirochetes, such as Vincent's angina, simple gingivitis, stomatitis, noma, alveolar abscesses, and pyorrhea alveolaris. These remedies may be used locally in 5 to 10 per cent. aqueous or glycerin solutions or even applied directly to the local lesion in powder form. They may also be used intravenously but only for severe cases with general symptoms, and for those that resist local treatment.

PEDIATRICS

UNDER THE CHARGE OF

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The Treatment of Scarlet Fever with Neo-salvarsan.—LOUIS FISCHER (*Archiv f. Pediatrics.*, 1913, xxx, 352) refers to the experiments in treating scarlet fever with intravenous injections of neo-salvarsan. Some cases of this disease give a positive Wassermann reaction and this has led a number of investigators to try the above treatment. Lenzmann, Schreiber, and others describe advantages by this treatment which indicate that a decided antipyretic effect is soon noted after the injection, and that there is a decided exfoliation of the necrotic membranes with tendency toward convalescence and absence of fatal complications. Infants received 0.1 gram, older children, 0.2 or 0.3 gram by intravenous injections. Some children required three or four injections. Arsenic alone, as in Fowler's solution was given in scarlet fever without result. Neosalvarsan is readily dissolved in water, shaking is not necessary, and it is a much more simple preparation than salvarsan. Fischer used this treatment in five cases of scarlet fever, all of which were septic and with a fatal prognosis. The Wassermann reaction was negative in three, one probably positive, and one unreported. Injections were given intravenously, the jugular vein being the best selection for giving the remedy. The dose employed was 0.2 gram in 40 c.c. of plain sterile water. No reaction such as shock, acute febrile attack, or rash followed the injection. Three of the cases died, but showed the antipyretic effect of the neosalvarsan. One case improved, following the injection and recovered, the credit of this being frankly given to the effect of the drug. One case was prolonged and is still in the hospital, but with a grave prognosis. While too early to make definite statements as to this treatment, enough has been accomplished to merit an extensive trial of this drug in scarlet fever.

The Etiology of Measles.—JEROME S. LEOPOLD (*Archiv. of Pediatrics*, 1913, xxx, 356) gives a *resume* of the work so far done in determining the etiology of measles. Anderson and Goldberger have proved the presence of the infectious agent in the blood and in the nasal and buccal secretions. Injection of blood from a measles case into monkeys caused characteristic eruption with fever, coryza, bronchitis, and often pneumonia. The infectivity of the blood was greatest shortly before the eruption of measles appeared, lasted twenty-four hours, and rapidly diminished. Hektoen successfully reproduced the disease in adults by subcutaneous inoculation with blood taken from measles cases during the first thirty hours of the eruption. The former investigators also obtained positive results by applying secretions from the mouth and pharynx of measles cases to the mouth and pharynx of monkeys. All attempts to inoculate monkeys with epi-

dermal scales of measles have failed. The virus is ultramicroscopic; desiccation is resisted for twenty-four hours, freezing resisted for twenty-five hours, and infectivity is destroyed by heating to 55° C. for fifteen minutes. All attempts to grow the virus are unsuccessful.

The Cause and Prevention of Adenoid Growths in Children.—H. E. JORDAN —*Archiv. of Pediatrics*, 1913, xxx, 468) believes that the enlargement of tonsils and adenoid growth are the effect of a fundamental, controllable factor, and that the concomitant morbid symptoms are indirectly the result of the enlargement. Increased functional demand causes enlargement of the structures and this demand is caused by mouth-breathing, induced by chronic nasal colds in children. The solution, then, is to promote nose-breathing, which is largely a matter of preventing colds. The ultimate factor in the production of colds is the almost universal inattention to damp linen. Small children are allowed to go "wet" for hours, especially at night. The series of links are damp clothes, exposure, with evaporation and possibly chill; nasal cold with obstruction of the nostrils, mouth-breathing and hypertrophy of lymphoid tissue. Mothers should be more carefully instructed in keeping children dry, and means should be devised to make this condition easier to regulate.

OBSTETRICS

UNDER THE CHARGE OF

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Hebostiotomy.—KRIWSKY (*Monatschr. f. Gebürts. u. Gynäk.*, 1913, xxxvii, No. 4) reports the case of a patient whose first labor was successfully terminated by forceps. In the second labor the child was stillborn; in the third labor a living child was obtained by forceps; and in the fourth labor hebostiotomy by Döderlein's method was done, and an unusually large and well developed child was delivered by forceps. This child died at four months. The pelvis had been enlarged by the previous operation, but hebostiotomy was repeated upon the right side, and a large living child was again delivered by forceps. This child died two years afterward. Eight months after the second operation the x-rays revealed the fact that but partial formation of bony tissue had occurred. The patient again came under observation when eight months pregnant, came into labor, and was delivered by Cesarean section, followed by sterilization. Both mother and child made a good recovery. Kriwsky has collected a considerable number of reported cases, showing 76 spontaneous births after hebostiotomy, 26 repeated operations, and 15 cases in which Cesarean section was substituted. He believes that the operation has a place in obstetric procedures, and that the true conjugate should be not less than 7

cm. He would not select it for cases in which the true conjugate was less than 7 cm., and preferably in multiparæ. The operation may be substituted for perforation if the surroundings are favorable for an aseptic operation. Döderlein's method is preferred, and no especial complications are to be expected during the puerperal period. Bony union through the severed ends forms very slowly, and in many cases does not develop. Permanent enlargement of the pelvis rarely occurs.

The Influence of the X-rays upon the Membranes.—KAWASOYE (*Zentralbl. f. Gynäk.*, 1913, No. 14) has experimented upon pregnant animals to ascertain the effect of the x-rays. No alterations were found in the membranes in the wall of the uterus, but the results of the x-rays were in 3 out of 7 cases the production of abortion or premature labor. The liver and spleen of the fetus showed necrosis. Caution should accordingly be exercised in using the x-rays upon pregnant patients.

Hematoma of the Abdominal Wall in Pregnancy.—VOGT (*Zentralbl. f. Gynäk.*, 1913, No. 14) reports the case of a young woman in her second pregnancy, who gave birth to a normal infant in spontaneous labor. Several hours after delivery the patient complained of severe pain above the symphysis. No alteration in the skin of the abdominal wall was evident. The uterus was at the umbilicus, well contracted, and little sensitive. Above the symphysis were two superficial tumors which could be moved upon the subjacent tissue. On further examination it was found that these were hematomas at the inferior extremity of the recti muscles. The tumors increased somewhat in size, and their absorption proceeded slowly. Four weeks elapsed before the patient was in normal condition. There was no explanation for their formation.

The Electrocardiogram in Pregnancy.—RUDNER (*Zentralbl. f. Gynäk.*, 1913, No. 13) has used the electrocardiogram in studying the condition of the heart in pregnant patients. Characteristic tracings were obtained which practically confirmed previous clinical observations. The value of the method lies in its graphic demonstration.

Uterus Bicornis Causing Chronic Transverse Position of the Fetus.—VON KLEIN (*Zentralbl. f. Gynäk.*, 1913, No. 13) reports 6 cases of uterus bicornis with transverse position of the fetus treated by version, and one by Cesarean section. It seems more than probable that this uterine abnormality is a frequent cause for transverse position.

The Correlation of the Internal Secretions of the Ductless Glands and the Genital Functions of Women.—BELL (*British Med. Jour.*, April 5, 1913) concludes in two lectures upon this subject, that although there are great variations in the structure of the ductless glands in different mammals, the total functional result is the same, so far as the genital processes are concerned. The individual metabolism of the mother and the metabolism of her reproductive functions are completely interdependent. While the ovaries furnish ova and keep

active the rest of the genital structures and functions, they are also concerned in keeping the other members of the ductless glands active, in relation to the necessity of the reproductive organs. When the reproductive functions cease, and the ovaries atrophy at the menopause, the general relationship is temporarily deranged, and various disturbances follow. It is only by the careful study of each individual case that one can learn in what manner the balance has been destroyed. The basis of treatment for the disorders of the menopause must be found in the disarrangement between the ovaries and the remaining ductless glands. Some patients are benefited by thyroid extract at the menopause; some by pituitary extract; others by various combinations. There is evidence that hyperplasia of the suprarenal cortex can offset the influence of the ovary and produce some of the secondary characteristics of the male in the female body, and partially change the development of the genital organs. The ovary influences the general metabolism in relation to its primary reproductive functions. The thyroid, pituitary, and suprarenals influence the development and preserve the integrity and activity of the genital organs. The thymus and possibly the pineal gland seem to prevent sexual precocity. All the ductless glands control metabolism in proportion to the necessities from the genital functions. When these cease the characteristic phenomena of the menopause develop. On the contrary, insufficiency of the thyroid, pituitary, or suprarenals, cause the genital functions to cease and the uterus to atrophy.

The Ovary as an Organ of Internal Secretion.—GRAVES (*Amer. Jour. Obstet.*, April, 1913) believes that in the present state of our knowledge anatomical evidence makes it probable that the ovary is an organ of internal secretion. Infantilism is not a result of ovarian deficiency, but is a manifestation of deficient development in which the ovary may or may not share. After sexual maturity the ovary has a trophic influence over the other genital organs. The ovaries preside over menstruation by an internal secretion which acts upon the endometrium. Abnormal uterine hemorrhage may be due to increased secretion of the ovaries. The transplantation of ovarian tissue has not proved to be of great practical value in the surgical treatment of gynecological cases. When the ovaries are removed from mature women, vasomotor disturbances follow in 80 per cent. of cases. The removal of the ovaries does not directly cause definite disturbance of the nervous system. If these symptoms are present, they are due to other causes. Ovarian extract is very valuable in treating the vasomotor disturbances which follow the removal of the ovaries. In other gynecological conditions it is of little importance.

The Mucous Channels and the Blood Stream as Alternative Routes of Infection.—BOND (*British Med. Jour.*, March 29, 1913), in a very interesting paper upon this subject, with illustrations, concludes that when an organism like the *Bacillus coli communis* reaches the pelvis of the kidney by ascending the urinary tract, it produces symptoms in effect which differ from those caused by the same germ that reaches the kidney by way of the blood stream. The organism seems to adapt itself to a mucous and urinary environment, on the one hand, and a blood or lymphatic channel, on the other.

GYNECOLOGY

UNDER THE CHARGE OF

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Treatment of Postoperative Retention of Urine.—The use of pituitrin in the treatment of urinary retention in women after operations and in the puerperium is very strongly recommended by EBELER (*Zeitschr. f. gyn. Urol.*, 1913, iv, 55), who has tried it in 21 puerperal and 24 postoperative cases, with excellent results, finding that by its use he was able in all cases to avoid catheterization. All the injections were given deep into the muscles; they are best given when the bladder is fairly full, and the patient feels the necessity of having it emptied. An injection of pituitrin given under these circumstances is nearly always followed within five minutes to ten minutes by an increased desire to micturate, this usually culminating in a spontaneous evacuation of the bladder; in some instances, however, this does not take place until after the lapse of a few hours. If the injection is given with the bladder only about half full, the action is less marked, but is still distinctly noticeable; if given when the bladder is empty, there is no appreciable effect whatever. Ebeler does not advise giving an injection upon the first intimation on the part of the patient of a desire to pass water, but thinks it is better to wait until there is very distinct discomfort in the bladder region. When once a voluntary micturition has been secured, it has seldom been found necessary to repeat the injection; in only 8 of Ebeler's 45 cases was a second dose required. In all instances the bladder was completely emptied, so far as could be determined by percussion, without using the catheter.

Treatment of Uterine Hemorrhage by the X-rays.—Although great activity along this line has been manifested in recent years throughout Europe, but comparatively little has appeared in the American literature upon the subject; a paper recently read before the Philadelphia Obstetrical Society by PFAHLER (*Amer. Jour. Obstet.*, 1913, lxxvii, 860), reporting a series of cases with exceedingly encouraging results, is therefore of considerable interest. This report comprises 23 cases of more or less severe uterine hemorrhage; in 21 of the patients fibroid tumors were present, the other 2 were examples of "metropathia," without demonstrable cause. In most instances a marked diminution in the size of the tumor was noticed following treatment, in addition to the effect produced upon the hemorrhage; indeed, in 12 out of the 16 patients who have ceased treatment, the tumor has entirely disappeared. In 2 of these patients, the growth extended to the umbilicus, but after five and four years respectively it can no longer be found. Pfahler says that he has never seen malignant degeneration of a myoma follow x-ray treatment, and does not consider the danger from this possibility very great. Where the patient is very anemic,

he always insists on rest in bed after the first series of treatments, as these are often followed by somewhat increased hemorrhage. In one of his cases treatment was followed by amenorrhea and disappearance of the tumor; after a time, however, menstruation was reëstablished in normal amount, and the patient has continued in perfect health. The treatment is given in series of from three to nine applications, generally on successive days, each series being followed by an intermission of about a month. If bleeding has not ceased after six treatment-series, the case should be considered unsuited for this form of therapy, and surgical intervention considered. Pfahler believes that the best results will be obtained if the cases are carefully selected by a trained gynecologist and treated by an expert Röntgenologist. He does not, as a rule, advise applying x-ray treatment to women aged under forty years, although in exceptional instances this may be permissible.

The Use and Abuse of the Curette.—In an article which FRANK states is intended primarily for the *general practitioner*, he (*New York Med. Jour.*, 1913, xcvi, 808) calls attention to the excessive fondness which apparently still exists among the profession for the curette, a condition which not infrequently leads to serious consequences. In running over the records of 2000 consecutive cases seen in his dispensary service, Frank has found that considerably over one-fifth of these women had at some time or other been curetted; several of the patients upon whom this operation had been performed were unmarried, or had not yet reached the age of puberty. Of 721 cases of abortion, either spontaneous or induced, nearly every second patient had been curetted; in 20 instances the operation had been performed post partum, in 32 cases sterility was the indication, in 36 menorrhagia or metrorrhagia, and in 40 leukorrhea. Frank considers that in practically all these cases the curette had better have been left unused. Whereas 50 per cent. of the cases curetted post abortum showed subsequently inflammatory lesions of the adnexa or parametrium, these were present in only 12 per cent. of an equal number not curetted. To curette post partum is, in Frank's opinion, never justifiable, as it only breaks down the natural defenses of the uterus, and opens wide paths of invasion to infectious organisms. While careful and light curettage post abortum may be justifiable, and at times even necessary when the patient is in a hospital, surrounded by all the facilities which it provides, Frank believes that the general practitioner will come out much better in the long run if he refrains from applying this treatment under the unfavorable conditions usually found in private practice, and adopts almost exclusively the purely expectant policy in treating these cases. He believes, further, that in the small percentage of cases in which curetting apparently does good in sterility or "endometritis" (*i. e.*, leukorrhea), it is really the preceding *dilatation* which has been of benefit. Frank does not wish to be misunderstood as desiring to banish the curette altogether, since it has, when properly used, a position of vital importance in our gynecological armamentarium; this position is as a diagnostic rather than as a therapeutic weapon, however. In cases of irregular bleeding—especially the climacteric and preclimacteric menorrhagias and metrorrhagias—it

should be obligatory on the attending physician to use the curette, but not so much with the expectation of curing the condition as of removing material for histological examination. He believes that were the profession as a whole fully alive to the importance of this point, the public could be educated within a couple of years to demand such an examination, just as they now demand a Wassermann test in suspected syphilis.

OTOLOGY

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The Function of the Auricle.—The widely varying opinions as to the acoustic and protective value of the human auricle are carefully presented by H. FRANKE (*Beitrage zur Anatomie, Physiologie, Pathologie, und Therapie des Ohres, der Nase, und des Halses*, vi, No. 3, 219) with a degree of detail which makes, in each instance, an abstract of the conclusion drawn from the recorded observation of the individual writer. The papers which form the basis of Franke's review, twenty-five in number, range from Buchanan in 1828 to the present day, and are widely divergent in their deductions; in some instances the auricle being regarded as of importance in the collection, the reflection, the reinforcement of sound waves, and as a resonator for certain tones and, moreover, of definite assistance in the determination of the direction of a sound source. Burkner, for example, in a case in which one auricle had been lost through accident, without injury to the middle, or internal ear, the tragus remaining uninjured, the hearing for the watch was found to be equal in the two ears so long as the sound source was held opposite the tested ear in the line of the long axis of the external auditory canal; a departure from this line, in any direction, exhibited a much more rapid falling off in the recorded hearing distance of the ear without an auricle, the conclusion of the observer being, naturally, that the auricle is important for the perception of sound by its collection of sound waves and their corresponding transmission of the sound waves to the middle ear mechanism and the perceptive apparatus. Burkner also found that with only the sound ear exposed the patient was accurate in his determination of the direction of a sound source, but that this was by no means the case when the perfect ear was tightly stopped and an attempt made to determine the direction of a sound source by means of the mutilated ear only. When both ears remained free the determination of the direction of a sound source was, in the majority of instances, correct, but more mistakes were noted when the sound came from the direction of the mutilated ear. Gradenigo drew similar conclusions from a corresponding case, observed by him, and confirmed the observations as to the lesser ability to determine the direction of a sound source on the affected side. Schaefer regards the human auricle as of funda-

mental and conclusive value to the hearing as a whole, reporting instances of progressive depreciation in the hearing power where the auricle had been mutilated or removed, and corresponding improvement in the hearing when means were taken to convey sound directly into the affected ear. Johannes Müller and Gigel, with other observers, concluded that the principal medium for the transmission of sound waves falling upon the auricle was through the substance of the auricular cartilage itself and its consequent conveyance along the tubal cartilage of the external auditory canal to the middle ear, instancing the hearing for tones of low pitch in auscultation either by contact of the auricle directly with the body of the patient or with a directly applied stethoscopic tube. Out of the material afforded by these observations, with the addition of his own, Franke arrives at the conclusion that the auricle has one well assured function, namely, the protection of the deeper portion of the ear, in which protection the tragus, extending over the meatus, plays an important part, but he makes no allusion to the caloric value of the auricle, the increase in its circulation when exposed to cold air serving to counteractively increase the temperature of the external auditory canal and helping to maintain the normal body temperature in the drumhead and in the middle ear. Franke further concludes, on the whole, that if the auricle in man is not to be regarded as a physiologically worthless rudimentary organ, it must be admitted to have but small value in the light of its contribution to the function of hearing.

The Relationship between the Hearing for the Whisper and the Conversational Tone.—Upon the basis of the observations in regard to functional hearing tests of Wolf, Bezold, Siebenmann, and others, JULIUS VEIS (*Archiv f. Ohrenheilkunde*, 1913, xc, 3) draws comparisons between the audible values of the human voice in ordinary conversational use and in a whisper, the former as representing tones of medium low and the latter tones of medium high pitch. For purposes of uniform testing in whispering, numerals were selected according to their presentation of low or high-pitched vowel sounds, thus affording a condensed means for speedy and accurate comparison in individual cases. The difficulty of determination of the relative pitch of whispered vowel sounds was confirmatory of the earlier observations of O. Wolf, this being in part due to the fact that the toneless whisper ranges far above the *medium fundamental tone* of ordinary speech, the latter being definitely a test for the medium low tones and the former for the medium high tones of the auditory scale; under these circumstances the voice test is both valuable for itself in the great majority of cases, and as an adjunct to the other forms of hearing test in common use. From his investigations carried out in cases of impairment of hearing from causes pertaining in both the middle and the internal ear, Veis draws the following conclusions: (1) The test of hearing by means of the conversation form in comparison with the parallel test in a whisper is important in cases of marked impairment of hearing (whisper less than 1m), in reference to diagnosis, therapeutics and prognosis; a test with the whispered voice alone gives no adequate determination of the actual hearing power. (2) In cases of otosclerosis and in many cases of past suppurative inflammation

of the middle ear the conversation tone was heard at a not much greater distance than the whisper, while in cases of labyrinthine deafness and in the exudative process of middle ear affection the conversation tone was heard far better than the whispered voice. (3) When the conversation tone is heard much better than the whisper there is more promise of improvement in the general hearing under treatment. (4) Improvement in hearing, in consequence of middle ear inflation, is evidenced mainly in regard to the conversation tone, the hearing for the whisper being either not at all or only slightly improved.

Clinical Observations upon a Hitherto Undescribed Form of Tuberculosis of the Middle Ear.—From a large material of cases of tuberculosis JOERGEN MOELLER (*Zeitschr. f. Ohrenheilkunde*, lxiv, 4) selected a series of cases of middle ear tuberculosis presenting symptoms the evidence and import of which seemed to have been heretofore unappreciated. In tuberculous patients who complain of no more serious symptoms than subjective noises or a diminution of hearing, objective examination shows in the early stage of the middle ear implication, appearances corresponding to those of a simple, acute, suppurative, middle ear process. The drumhead was distended, the long process of the malleus lay in a furrow or was entirely concealed by the distention of the drumhead outward, the color of the membrane was a yellowish-white, dull, and not diffusely injected as is the case in simple acute inflammation of the middle ear, but instead, against the dull yellowish white background there was a network of distended bloodvessels radiating from the manubrial plexus. Inflation of the middle ear by means of the air douch gave only temporary and partial relief from the subjective symptoms and paracentesis revealed a dry incision through a generally thickened membrane, an opening which was usually entirely healed on the following day. As a rule, in a majority of the cases, the inflammatory process either resolved or localized itself in one spot, or another of the drumhead, as a small and limited ulceration confined to only one layer of the drumhead while in other instances the necrotic process was more general in its attack, the drumhead became perforated, and the subsequent course of the case was that of the ordinary suppurative middle ear tuberculosis. The implication of the middle ear throughout evidenced itself as primarily a diffuse tuberculous infiltration of the drumhead and of the tympanic mucosa, this view being supported by the histological examination of excised portions of the drumhead.

Temporary Glycosuria in the Course of Suppurative Middle Ear Disease.—Upon the basis of the following experience ALFRED ZIMMERMANN (*Zeitschr. f. Ohrenheilkunde*, lxvii, Nos. 3 and 4, 217) was led to make an extended review of the literature concerning the question of the relationship of the presence of sugar in the urine for short periods, during the progress of a suppurative process in the middle ear. The patient was a man, aged twenty-four years, who, in sequence of a cauterization of the left inferior turbinate, had, two days later, an acute inflammation of the right, middle ear from which paracentesis of the drumhead liberated a serous discharge; there was also

a light implication of the left ear; on the following day there was a slight further rise in temperature and a copious purulent discharge from the right ear exhibiting, both microscopically and by culture, staphylococcus, streptococcus, and psuedodiphtheria bacillus. The congestion of the left middle ear rapidly decreased with an ultimate return to normal, but in the right ear continued and increased, but without evidence of intracranial complications. The urine, as examined when the case was first seen, was practically normal, without a trace of albumin or of sugar, but on the seventh day, under the same dietary conditions as before, a large percentage of sugar was found in the urine. In the subsequent course of the case, with a gradual decrease in the local, aural, disturbance, the percentage of sugar proportionately decreased, and finally disappeared notwithstanding a resumption of the ordinary diet which had, for a time, been suspended. Beginning with the investigations of Claude Bernard upon the effect of injury in the region of the floor of the fourth ventricle upon sugar elimination, and following through the clinical literature of the subject, Zimmermann concludes that suppurative inflammation of the middle ear, even when it does not extend beyond the boundary of the temporal bone, especially at the acme of its clinical evidence of activity, may be the cause of a transitory glycosuria which should in no way be confounded with, or lead to an oversight of, the really serious renal lesion of which this symptom might be an evidence.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Bordet-Gengou Bacillus of Whooping Cough.—MALLORY, HORNER, and HENDERSON (*Jour. Med. Research*, March 1913) have completed the proof according to Koch's postulates that the recently described bacillus is the actual cause of whooping cough. They have been able from sputum to obtain pure cultures, to produce the lesions which they have shown to be characteristic in young animals, and in four instances have obtained the organism again from these subjects in pure cultures. They consider that a vaccine or antitoxin is probably within reach.

The Effect of the Spleen and Splenic Extract upon Malignant Tumors.—OSER and PRIBRAM, from Prof. v. Eiselsberg's clinic (*Zeitschr. f. Exper. Path. u. Ther.*, January, 1913, Band xii, Heft 2) undertook experimental work upon the effects that can be produced on malignant tumors by the absence of the spleen as well as by splenic

extracts. Oestrich had supposed that chondroitin-sulphuric acid was responsible for certain favorable effects on carcinomatous growths, and Oser and Pribram used his medium, composed of sodium chondroitin-sulphate and β -eucaine, upon a series of patients, but were entirely disappointed by the lack of good results. Considering that the spleen is almost as efficient as the bone marrow as a site of formation for antibodies, and that agglutinins can be demonstrated in the spleen earlier than in the blood, Braunstein obtained good results by removing the sterile spleen from cancer-mice and injecting the extract of the spleen in salt solution into other cancer-mice. He first used mice which had been injected with carcinoma, and removed the spleen before any tumor appeared. Of other cancer-mice so injected, one-fourth of those surviving showed tumor recession. One-third died of the injection. When he took the spleen from mice with well developed tumors, 6 of 15 mice injected died, but 5 of the remaining 11 showed recession. Yet again, he took the spleen from mice injected intraperitoneally repeatedly with carcinoma and sarcoma extract, four to six days earlier; this was injected into 45 cancer-mice with 3 deaths; in 6 recession of growth occurred, in 3 cessation of growth. Of 7 sarcoma-rats similarly tested, 6 showed regression. Braunstein's conclusions were that the spleen possesses a highly developed power of resistance against tumor growth, while, on the contrary, splenectomized animals are more liable than normal animals to the inroads of malignant growth. Rohdenberg and Johnston made observations that were parallel upon the thymus, pancreas, spleen, hypophysis, and testes, showing that after extirpation of the thyroid, thymus or testes the animal had a lessened resistance to carcinoma. Oser and Pribram's experiments support the views of Braunstein, and they show measurements and pictures of tumors indicating regression, and also the comparatively quicker growth of tumors in previously splenectomized animals. Spleen extract was efficient in the possession of antibodies, while blood removed at the same time failed to show such qualities.

Anaphylotoxin, Peptotoxin, and Anaphylaxis. — BESREDKA, STRÖBEL, and JUPILLE (*Annal. de l'Inst. Pasteur*, March, 1913, xxvii, No. 3) give details of some interesting experiments upon anaphylotoxine, a name which Friedberger gives to what he supposes to be the active agent in anaphylaxis; he considers that the anaphylactic state of an animal with regard to an albumin is due to the appearance of precipitin in its serum, and anaphylactic shock is the result of combination of the precipitin with the alexine of the animal. This being the case, one had only to inject an unprepared animal with the test-tube preparation of precipitin and alexin, and the result showed that the intravenous injection was highly toxic to the animal. This substance Friedberger called *anaphylotoxine*. In the words of Besredka, Ströbel, and Jupille, "the fortune of anaphylotoxin was made, and almost any bacillus, however slightly pathogenic, could apparently be proved to possess its anaphylotoxin." We were in a fair way to find that even infectious diseases were the work, not of specific pathogenic agents so much as of anaphylotoxin. Besredka, Ströbel, and Jupille have endeavored to stem the triumphant march of the ana-

phylotoxins by attempting to find out if they are the specific poisons of anaphylaxis. To obtain a microbial anaphylaxis, it was necessary to make an alexin act on microbes and specific serum; it was then discovered that specific serum was unnecessary, and that it sufficed to make the alexin act on the bacilli alone. Still later the authors have simplified the technique by withdrawing from it the bacilli, making the alexin act on the sterile medium without bacilli; they have obtained thus a toxic substance which has all the characters of anaphylotoxin. This they have called peptotoxin because of its relationship with peptones, in preference to anaphylotoxin, since they consider it to have no relation to anaphylaxis. For purposes of comparison they have taken guinea-pigs injected with anaphylotoxin, peptotoxin, and peptone, followed by bacterial vaccination in progressively increasing doses quickly administered. The results have been to show that anaphylotoxic shock and anaphylactic shock are two entirely different things, and that vaccination following anaphylotoxin, peptotoxin, and peptone, presents well-defined characters common to these three substances, and very distinct from the characters which designate the ordinary anti-anaphylaxis. The toxic effects produced by the peptone and its derivatives may exactly copy the effects of anaphylaxis, but the "peptonic shock" does not in the guinea-pig produce any protection against anaphylactic shock. Typhus anaphylotoxin can be injected safely into the venous system in guinea-pigs in increasing doses, injected at short intervals, and the same is true of peptotoxin and of the peptone; in all three cases, however, the weight of the animal and the dose of poison must be reasonably coördinated, and for all three it is likewise necessary that the venous circulation should be used. Anti-anaphylactic vaccination does not possess these characters, and Besredka, Ströbel, and Jupille conclude that the phenomena which they attribute to anaphylotoxin, peptotoxin, and peptone have nothing in common with true anaphylaxis. We are thus, they think, carried back once more to our original conception of anaphylaxis and anaphylactic shock, which excludes the idea of intoxication by a particular substance such as anaphylotoxin. They compare the process of desensitization which occurs during the anaphylactic state to a rapid decoloration or decompression: when such decompression or decoloration occurs in a gradual and progressive manner, the process of anti-anaphylaxis is being accomplished.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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THE
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SEPTEMBER, 1913

ORIGINAL ARTICLES

A LOBAR FORM OF BRONCHOPNEUMONIA OF LONG DURATION, OCCURRING IN CHILDREN AND YOUNG ADULTS.¹

BY DAVID RIESMAN, M.D.,

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FOR some time, possibly four or five years, I have been interested in a disease of the lungs which cannot be readily classified nor easily named.

CASE I.—The first case I saw was in a young girl, who came to the dispensary of the Polyclinic Hospital and puzzled my colleagues and myself by a long-continued, low fever. Week after week on her visits to the clinic we noted a moderate elevation of temperature, and as she had a cough, was pale and of poor physique, tuberculosis was naturally suspected. But aside from failure to find any evidence in the sputum, the physical signs—an abundance of crackling rales—were strictly limited to one lower lobe, there being no involvement of the apices. The history did not suggest an unresolving lobar pneumonia, and the child, so far as I can recall—the record is now lost—was not confined to bed at any time. After a most protracted course, covering possibly two or three months, the girl recovered completely.

CASE II.—On September 12, 1911, I saw in my office Pearl L., a girl, aged thirteen years, who had been coughing for two weeks. At the age of two years she had whooping cough, otherwise she had been well. Although she did not appear to be very ill, I found impairment of resonance over the entire left lower lobe and sharply limited to it. The breath sounds were harsh and of a broncho-

¹ Read at the meeting of the Association of American Physicians, May 8, 1913. A preliminary report was made to the College of Physicians of Philadelphia on February 5, 1913.

vesicular character. There were also numerous crackling rales. The right side as well as the upper lobe of the left lung was entirely normal. Temperature, 99.5°; pulse, 120. Four days later the signs were more marked, the involvement extending from the base of the left lobe to a little above the middle of the left scapula, and from the spinal column to the postaxillary line. The impairment was, however, very slight, and only discoverable by careful comparison of the two sides. The rales were of a coarse, moist type; temperature, 98.9°; pulse, 108. On her next two visits very few rales could be detected. On October 27, six weeks after I first saw her and eight weeks after the beginning of her illness, rather coarse rales confined entirely to the left lower lobe could still be heard. On November 22, no rales could be found, but as late as January 4, 1912, four months or more after the onset of the disease, the breath sounds over the left base were still a little harsh. I saw the girl again February 17, 1912, for some trifling condition, and at that time the lungs were clear.

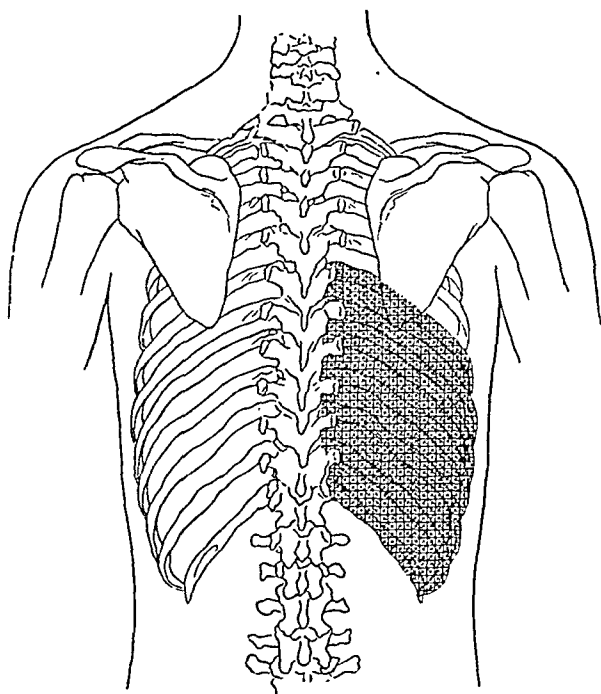


FIG. 1.—Bertha M. Impairment of resonance; bronchovesicular breathing; crackling rales; right lower lobe.

CASE III.—Bertha M., aged nineteen years, a Normal School girl, came to see me March 31, 1911, on account of a severe cough from which she had suffered on and off for three months. She is very robust and comes of healthy stock. The cough had "somewhat run her down," to use her own words. Temperature, 100.5°; pulse, 120. On examination I found impairment of resonance over the right chest from the angle of the scapula to the base. Over this

area the vocal fremitus was a little increased. On auscultation over the entire lower right lobe posteriorly, laterally, and in front from the mammary region down, numerous crackling rales could be heard. The lung elsewhere was normal. (Fig. 1.) The patient had no expectoration, the appetite was diminished, the bowels constipated. By April 8, only a few dry rales remained at the base of the right chest.

CASE IV.—Bernice B., aged six years, had whooping cough soon after birth, a mastoid operation and adenectomy at three, otherwise nothing except slight anemia and transient choreiform movements. I saw her first on May 28, 1912. She had been coughing for some time. On June 6, I noted in my records: Cough very hard; temperature, 99.4°; harsh breathing at left base. On June 10: Cough continues; temperature, 99.4°; slight impairment of the percussion note of the left lower lobe posteriorly and in the axillary region, with harsh breathing and a fair number of fine rales. On June 17 the notes state: Temperature normal; cough less severe; rales have nearly all disappeared.

CASE V.—Dora Y., aged thirteen years, was seen with Dr. Hofkin on June 27, 1912, the history being that she had been ill with a continued fever for some time; just how long I could not ascertain. Typhoid fever and tuberculosis had been suspected. There was no cough; no expectoration; the fever was moderate; at no time had the child seemed very ill. A few weeks before she was taken sick an uncle had died in the same house of lobar pneumonia. Examination of the patient, who was up and about, showed slight impairment of resonance over the entire lower right lobe posteriorly and in the axillary region. The vocal fremitus was not altered. On auscultation a tremendous shower of crackling rales, which became a little finer after coughing, could be heard. Inspiration was harsh and expiration somewhat prolonged, but not bronchial. I ventured the positive statement that the child did not have tuberculosis and would recover fully. In September Dr. Hofkin wrote to me that the girl had been taken to Atlantic City and that he had found the lungs clear five weeks after our consultation, but had noted the persistence of harsh breathing over the formerly affected lobe. When he reexamined her in September not the slightest abnormality could be detected.

CASE VI.—Sarah R., a girl aged twelve years, was first seen October 20, 1912. For three or four weeks she had had a severe cough, with some expectoration. According to the mother the child had been subject to such attacks for several winters, and when once started they would last throughout the cold season. The cough was worse at night and often disturbed the child's sleep. There were no night-sweats. The family history was good, and as for the patient, aside from the winter cough, she had had nothing except chickenpox at the age of two years. Examination showed

over the left lung posteriorly a slight impairment of resonance. On auscultation numerous dry and some moist rales could be heard over the lower lobe of the left lung, behind and as far forward as the midaxillary region. (Fig. 2.) Nowhere else were any abnormal sounds to be detected. The heart was normal; the spleen not enlarged; temperature, 98° ; pulse, 80. A few days later the patient had a severe stitch in the left side with a catch in breathing. When I saw her on October 27, there was no friction sound. The resonance over the left lower lobe was still a trifle impaired; the rales had disappeared.

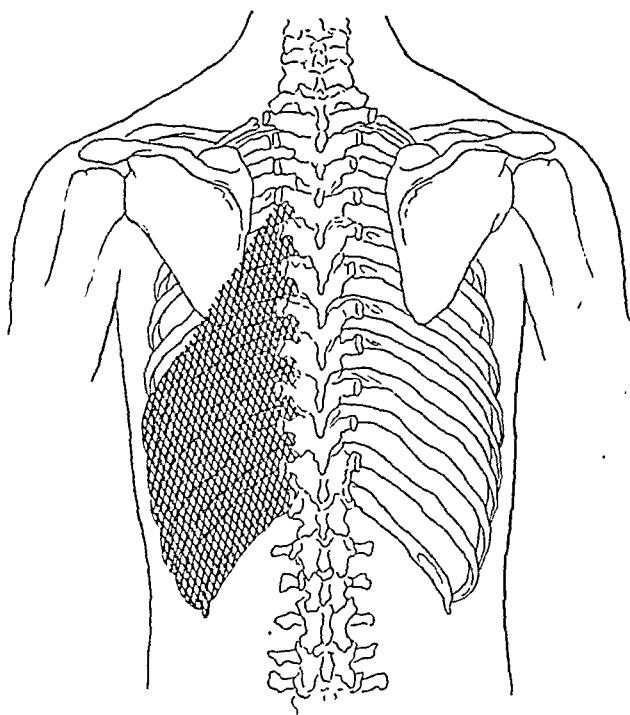


FIG. 2.—Sarah R. Impairment of resonance; bronchovesicular breathing; crackling rales; left lower lobe. Posterior view.

CASE VII.—W. N., a colored lad, aged fourteen years, was sent to me by Dr. Watson, at the Polyclinic Hospital, on March 1 of this year, because, just as he was about to undergo an operation for enlarged tonsils, it was discovered that he had a temperature of 100° . The boy had had diphtheria at the age of seven and frequent attacks of tonsillitis. He did not complain of anything, but after we had detected the physical signs about to be described he admitted that for a week past he had had a slight cough, without expectoration, and some headache. I wish I could picture to you the surprise of my group of postgraduate students—and my own—when upon examination we found over the lower lobe of the left lung many small moist rales, bronchovesicular breathing, and impairment of the percussion note. (Fig. 3.) There was nothing

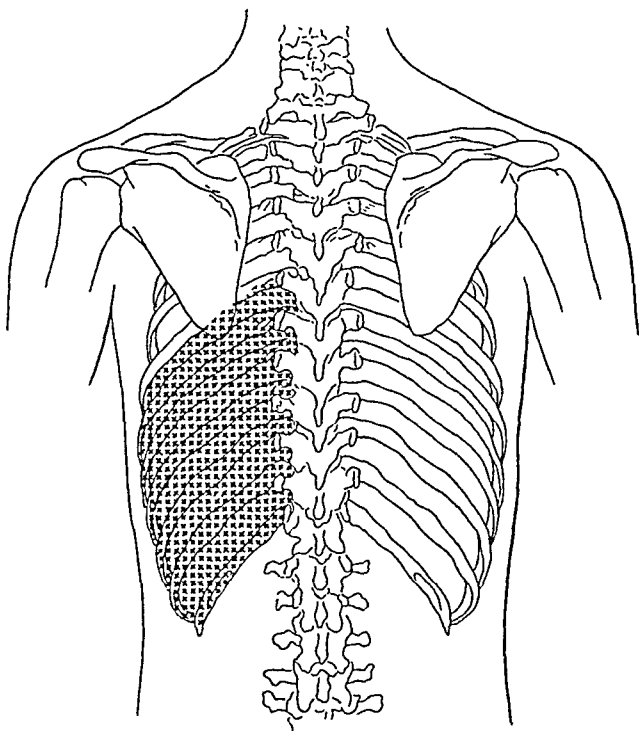


FIG. 3.—W. N. Impairment of resonance; bronchovesicular breathing; crackling rales; left lower lobe.

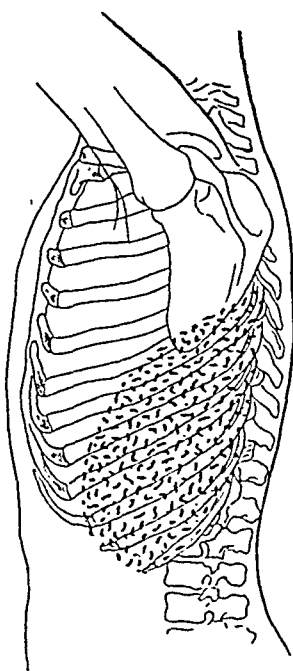


FIG. 4.—Dr. H. Impairment of resonance; bronchovesicular breathing; crackling rales; left lower lobe. Lateral view.

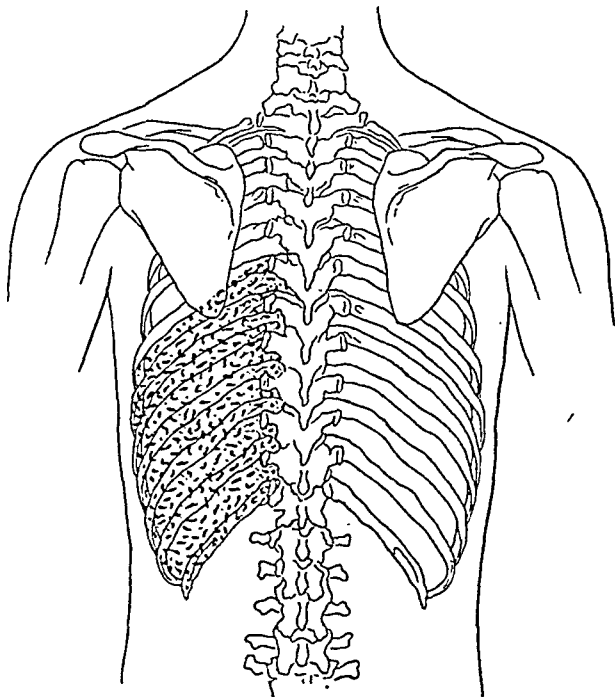


FIG. 5.—Same case as Fig. 4. Posterior view.

in the history, in the symptoms, or in the general impression that the boy made upon us to suggest any trouble in the lung. Had it not been for our practice of making a routine examination of the posterior bases of the lung the trouble would surely have been overlooked. It is not improbable that some of the ether pneumonias are preceded by just such a condition as we found in this boy. If that is true then it behooves us in every case before an operation to make a thorough examination of the back of the chest.

The blood count gave the following results:

Hemoglobin	88 per cent.
Red cells	5,320,000
Leukocytes	16,160
Differential count:	
Polymorphonuclear cells	57.4 per cent.
Mononuclear cells	7.0 "
Small lymphocytes	28.6 "
Transitional	5.4 "
Eosinophiles	1.6 "

At the end of three weeks from the time he was first seen the boy was entirely well.

I have cited the foregoing seven cases as typical of the disease. I have seen perhaps double that number.

PATHOLOGY. There have been no autopsies and no *x-ray* examinations, so that the actual pathological anatomy is an inference. The condition is not an ordinary bronchitis: (1) because it is strictly unilateral, while bronchitis is generally bilateral; and (2) because unlike bronchitis it is accompanied by an impairment of the percussion note and by breathing of a bronchovesicular character. Repeated examination in my cases has shown the physical signs to be quite stationary in the part first affected. Nor can the condition be a pleurisy: the signs remain unchanged, no fluid is demonstrable, the tactile fremitus is either not altered or increased, and the line of dulness follows the slant of the division between the lobes and has not the characteristic curve of an effusion. There is also practically no pain.

It is not a lobar pneumonia of the ordinary type, for it has not the acute, sharp onset, nor does it at any time give the impression that there is complete consolidation of the lung.

The view that we are dealing with a lobular or catarrhal pneumonia becoming confluent and assuming a lobar distribution seems to me to accord best with the conditions present. While lobular pneumonia in the vast majority of cases is a bilateral process, there is no inherent reason why it may not be unilateral. As the modes of infection in the two forms of pneumonia are not unlike; and as the infecting organism is generally the same, it is well within the law of probability that lobular pneumonia may be confined to the same parts of the lung as lobar pneumonia. Since we possess no

satisfactory explanation for the lobar distribution in the one, none can be demanded for a similar distribution in the other.

In some experiments with the pneumococcus, Dr. Kolmer and myself, using the Lamar-Meltzer method, produced in dogs a pneumonia confined to a single lobe that to our minds had the characteristics of a spreading lobular rather than of a true lobar pneumonia, thus bearing a close analogy to the disease under discussion. At best, however, the pathological differences between lobular pneumonia and lobar pneumonia are neither great nor important.

It has not been possible to obtain sputum in many of the cases. When it was obtained it showed chiefly pneumococci. That the pneumococcus is capable of causing not only acute but also chronic pulmonary infections is demonstrated by the painstaking researches of Leutscher.

There is no evidence that the condition is an interstitial pneumonia of the type so ably described by Dr. Jacobi,² for it heals without residue—without evidence of retraction.

The disease would not impress anyone as a manifestation of influenza. The cases I have seen were scattered over a considerable period of time. They had none of the catarrhal symptoms nor the prostration so characteristic of influenza. Moreover, no other members of the patients' families were affected.

The chief symptoms are cough and a moderate fever, rarely above 101°, extending over a long period—from several weeks to three or four months. The cough may be harassing, but at times is slight, scarcely of enough moment to attract attention. There may be considerable expectoration or none; it may contain a little blood, but in my experience has never been rust-colored. The physical signs are entirely out of proportion to the symptoms. There is always some dulness, which is most easily detected by a careful comparison of the two sides, and usually extends to the angle or the middle of the scapula. Rales are, as a rule, abundant, and of the peculiar quality best described as consonating. They are moist rather than dry, though both types may be found. In the presence of minor subjective symptoms the listener will often be surprised when approaching the base of the chest to find his ear bombarded by a chorus of exquisitely crackling sounds. The rales are heard best in inspiration, and are often increased by coughing. In the majority of cases the disease involves the lower lobe of the left lung, but this may be a mere coincidence, as the number of cases is as yet too small for a definite conclusion. Girls predominated among my patients. As to age, the majority were between ten and twenty years—one was twenty-seven and one twenty-eight years. All the cases have ended in recovery without a vestige of the morbid process remaining.

² Arch. Ped., January, 1903.

On looking, not exhaustively, through the literature I find nothing directly bearing upon the subject. A number of authors in their chapters on bronchopneumonia state that at times the disease is most marked in one lobe, and when confluent may simulate lobar pneumonia. Such types are, however, described as exceptionally severe, with high fever, marked dyspnea, profound prostration, and great danger to life. They differ thus radically from the disease with which we are dealing. Beddard³ speaks of a primary lobular pneumonia which is usually confluent and is diagnosticated as lobar. This, however, has a sudden onset, with high temperature and severe nervous symptoms; the duration is short, the pyrexia is quite regular and sustained, and it often ends by crisis. This, of course, does not correspond to our disease. West⁴ described three types of bronchopneumonia, none of which is identical with the one under consideration; although he recognized a secondary bronchopneumonia, not, however, of lobar type, with a protracted course lasting three months or more. The nearest approach is found in Powell and Hartley's book.⁵ They speak of a confluent form involving adjacent lobes of a large portion of the lung, sometimes a whole lobe, producing more or less dense consolidation. It may be associated with ordinary bronchitis of catarrhal origin, and very often occurs in the course of whooping cough. They have also met with it in certain cases of heart disease, and as a complication in pulmonary tuberculosis. In none of my cases was whooping cough, heart disease, or pulmonary tuberculosis a factor in the process; moreover, in severity and course the condition described by Powell and Hartley and the one here discussed are very different. Babcock⁶ recognizes a confluent bronchopneumonia, but does not go into details regarding the symptoms or course. Wilson Fox does not mention it.

TREATMENT. In the treatment the measures that have seemed to me of some avail are counter-irritation to the chest, abundant feeding, and either a simple cough mixture with a small dose of an opiate, or one of the creosote preparations. Whenever the weather was favorable I advised that the patient be taken outdoors. A sojourn at the seashore in proper season is also beneficial.

The essential features of the condition I have described may be epitomized as follows:

1. The disease is a confluent lobular pneumonia of lobar distribution characterized by long duration, low fever, and the following physical signs: impairment of resonance, bronchovesicular breathing, and showers of crackling rales.

2. It must be looked upon as one of the causes of obscure long-continued fever.

³ Allbutt and Rolleston's *System of Medicine*, vol. v, London, 1909.

⁴ *Diseases of the Organs of Respiration*.

⁵ *Diseases of the Lungs*, 1911, fifth edition.

⁶ *Ibid.*, New York, 1907.

3. The disease always seems to end in complete recovery both symptomatically and anatomically.

4. In the beginning typhoid fever may be suspected, in the later stages tuberculosis.

5. The disease is, I believe, often overlooked, due to the fact that we seldom examine the lower posterior aspects of the chest in ambulatory cases, especially when the symptoms are rather trivial. I am quite sure the diagnosis of tuberculosis is often made in these cases of chronic cough, with low, continued fever; but if the chest is carefully examined, back and front, above and below, the peculiar, almost specific character of the disease will be discovered, and then the thought of tuberculosis will be no longer entertained.

THE TRUE VALUE OF OPERATION FOR CANCER.

BY EDWARD MILTON FOOTE, M.D.,

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IN order to estimate the true value of operation for cancer, we must know (1) the object of the operation, and (2) its result. It is often assumed that there is only one reason for such an operation—namely, the removal of all diseased tissue. This is the so-called radical operation. Its range has been extended to include not only the visibly diseased tissues, but also those tissues which may have in them seeds of disease for future development, and especially adjacent lymph glands and fascial planes. This side of the subject has been thoroughly studied and its technical applications to the various cancer sites of the body repeatedly described. In fact, it may justly be said to have dominated the surgical mind, determining the type of operation and classifying the results. Important as attempted removal of the cancerous and precancerous tissues may be, this is by no means the only reason for operation in cancer, and it is manifestly an absurdity to follow blindly methods of technique worked out for a radical operation when the possibility of radical operation does not exist. Rather should one shape the operation in each case to the objects to be gained by operation in that particular case.

Speaking broadly, there are four reasons for operation for cancer which may be present in the mind of patient or surgeon:

1. The complete removal of the cancer and cancer-bearing tissue—the so-called radical cure.

2. The establishment of a diagnosis.

3. The relief of some special symptom, such as hemorrhage or discharge from an ulcerating surface, or the closure of a sinus, or the division of a stricture, or the removal of a disfigurement.

4. The attainment of certain social ends—to keep up the patient's hope or to satisfy the family that something is being done, etc.

One is tempted to add another reason, which probably exists in the mind of the patient and his friends oftener than they would like to admit, and that is the possibility that the patient may die from operation. But if this is admitted as a reason for operation, it will take its place among the social ends in class four.

It is obvious that the choice of operation should depend in no small degree upon which of these four reasons exists. The first reason—namely, the possibility of a complete removal of the growth—justly outweighs all other considerations when it is present. In order to accomplish this end the radical operations have been made more and more extensive, with a corresponding increase in operative mortality and postoperative debility. It is manifest that this tendency can be carried too far, that the price paid for possible immunity may be too great, especially in the case of a tumor beyond the earliest stage. The more extensive the growth the more extensive must be the operation, and the greater will be the operative risk, while the chance of a radical cure grows less and less.

The second object for which one may operate in cancer is the establishment of a diagnosis. If the growth is small it may be entirely removed, so that diagnosis and complete removal are effected at the same time. But this double object can only be attained satisfactorily in the case of small growths of limited malignancy, such as beginning epitheliomas of the skin away from the orifices of the body, so situated that it is practical to remove a fair margin of sound skin with the tumor. On the other hand if one removes in this way a small tumor of the breast, and it proves to be a commencing carcinoma and not a fibroadenoma, the requirements of a radical operation will not have been satisfied.

The field of the diagnostic operation has been narrowed in another way. It was once believed that a small portion of a tumor could safely be extracted by a punch or cut out through a small incision and submitted to microscopic examination. Such methods of examination are not looked upon with favor at the present time, certainly not in the earlier stages of a cancer or suspected cancer. The examination of a small piece of tissue may give misleading results, especially in incipient or doubtful cases, where a wrong diagnosis will do the most harm. Furthermore, cutting or punching through the normal tissue planes which surround a malignant growth has in some cases hastened its spread into these new planes, so that this risk has to be considered in such a diagnostic procedure, and it is generally conceded that patients should not be subjected to this risk unless they are beyond the possibility of a radical operation.

Another and better form of diagnostic operation is the exposure of a tumor, the examination of a portion of it by frozen section, and the completion of operation according to the report of the pathologist. Here the risk is that of an added delay of ten to thirty minutes for the pathologic examination. In many cases this is negligible, and the time can be reduced to a minimum, even below that mentioned, with practice in good surroundings. Some have made the claim that this technique exposes the patient to a dissemination of his cancer even though a radical removal is at once carried out. Such an extreme statement is not susceptible of proof and most surgeons have refused to be influenced by it. There are, however, limitations to the method. It should not be employed with patients too weak to endure the necessary delay with safety, and the section should always be removed in such a way that the wound can be properly closed if further operation is decided against. For example, one would not be justified in removing a section of the wall of a possibly cancerous stomach and then leaving the patient with a fistula. No diagnosis is worth such a price. There are also two technical limitations of this diagnostic method which should be fully admitted. It may be impossible for the surgeon to select for such examination the essential part of the tumor. There are instances in which dozens of sections have been made through inflammatory or other non-malignant tissue before the cancer was revealed. Again, some tumors are of such a nature that a correct diagnosis cannot be made by a few minutes' study of hastily prepared sections. Admitting all these limitations the method is of much real value, and is often of the greatest aid to the patient or his friends in deciding upon a radical operation.

Operation for cancer which is beyond the probability of radical removal is a subject worthy of more careful study than it has yet received. For practical purposes the special reasons for operation suggested under classes three and four are grouped together, for the social reasons for operation, no matter how urgent they may be, are almost always dependent upon some distressing physical condition; so in order to meet the social requirements the operation must be planned to relieve the physical distress.

But what is the usual procedure when a patient comes with an advanced primary growth, or with a recurrence, and asks for help? The surgeon, according to his temperament, gives a rosy prognosis or a guarded one. At all events he promises to do what he can. Now what he does is usually to follow the technique of a radical operation, just as far as he thinks the patient's recuperative power will permit, and then closes the wound as best he may; perhaps saying to himself or to an assistant, "Well, I got the most of that out."

This whole conception of operation under such circumstances is wrong. One should rather analyze the case and adapt his pro-

cedure to meet the difficulties which are present. There is the patient's dread of his disease and the fear that it cannot be removed by operation. Any operation well performed, with suitable mental suggestion, will allay this fear for a time; but few patients are today so uneducated or so simple as to give up all their fear at the command of the surgeon. Only returning strength for a long period after an operation will give them full confidence. All the patients in the class we are now considering are doomed to disappointment within a year or so in respect to a complete cure. Hence a prompt recovery from operation and good health for as long a period as possible are the chief aims of the operation—not the removal of extensive fascial planes, which at a late date may become cancerous, provided the patient lives long enough.

One cannot hope to formulate specific rules to cover the wide variety of conditions which cases of advanced cancer present to the operator, but there are certain general principles which ought certainly to be regarded.

1. The removal of the visible growth is desirable so far as this can be accomplished without sacrificing important muscles, nerves, etc. Although one need not feel obliged to remove so wide a margin of sound tissue as is the rule in the radical operation the natural limits of the growth should be removed with it whenever possible. For example, if it is attached to periosteum the periosteum should be removed too. If it infiltrates a muscle at least the affected part of that muscle should be removed. To cut through a cancerous nodule or gland and leave a half or a third of it behind is most unfortunate, and yet the limitations of this type of operation sometimes compel one to do this very thing.

2. The wound should be so shaped that it can be entirely closed. Skin grafts or a granulating wound are allowable in a radical operation, whereas a partial operation, which leaves a patient with a cancerous ulcer which did not previously exist, must usually be accounted a failure. If drainage is required it should be such that there will be no permanent sinus whenever this can possibly be accomplished.

3. Lymph glands should be removed if they are readily accessible, even if deeper ones which are known to be involved are left behind. Thus in some cases of carcinoma of the breast, with axillary glands involved in chains running up to the points where the vessels perforate the chest, the patient derives more benefit from a moderate clearing out of the axilla with preservation of at least a part of the pectoral muscles, and plenty of skin to close the wound, than she does from an extensive operation, with its higher mortality, longer convalescence, and limited usefulness of the arm. Why not let such a patient get up in five days, leave off bandages in ten days, and enjoy good health for a year or perhaps more, than to squander her potentials of happiness in an

effort to reach the unattainable? Let us adapt the operation to the conditions of the patient, or, in other words, to keep in mind while operating the true value of the operation for that particular individual.

4. It is of the utmost importance to save the patient's vitality by making the operation short, keeping the body warm, using a minimum of anesthetic, and above everything else, by keeping the loss of blood down to the smallest possible point. Such a patient's blood is his capital, which if lost he can replace only in a slight degree. The operator who squanders this blood capital therefore does him an irreparable injury. The careful operator will so perform his work that in most cases within a few days the patient will be able to enter into such enjoyment of life as conditions permit. An operation which entails a convalescence extending over weeks or months may be worth while if it promises even a chance of life prolonged for many years. If a patient has at the best only six months or a year of comfort before him it is obviously bad management to compel him to devote a quarter of that time to recovering from an operative shock, especially when there is the added fact to be reckoned with that the limit of his power to recover is easily exceeded.

5. If operation is performed for a special object, such as the relief of a plastic defect or to reduce the size of the mouth so that the saliva will not escape or to close a sinus in the cheek or to lessen the blood supply of the cancer, it is generally wise to limit the operation to its particular object, resisting the temptation to excise a few portions of the tumor because they are easily reached. Such excisions, unless they are so made as to include the growing edge of that part of the tumor, are often worse than useless, as they waste the patient's blood and do not prevent recurrence for a period long enough to repay him.

6. Plastic operations involving skin which is actually in contact with a cancerous growth may be successfully performed, and in case of slowly growing tumors they are often well worth while. There are instances in which such patchwork frequently repeated has kept a patient comfortable and more or less presentable for years after the possibility of any radical removal was exhausted.

7. Curettage or scraping of an ulcerating cancer is of doubtful efficacy. Sometimes it may be of use in checking hemorrhage, but usually it causes a positive blood loss at the time of its performance which can ill be spared. Its bad results are more noticeable in the case of rapidly growing tumors, in which it may fail to give the patient even temporary relief.

In order to estimate the true value of operation for cancer we must know first the object of the operation and next its result. This brings us to the second part of our subject. In looking over the published reports of work in this field we are again struck with

the fact that the possibility or failure of a radical cure dominates the surgical mind both in performance of operation and consideration of results. One may readily admit that duration of life following operation and freedom from recurrence are indeed the two great important facts which can be readily tabulated, and about which there can be little difference of opinion. But to the patient, improved function and improved appearance are equally important facts, although very difficult to tabulate or record accurately. The Scotch have a saying that "No man should thin his own turnips." Truth would be the gainer if no man estimated his own operative results, and yet in most cases no one else can do so.

In the records of these cases every endeavor has been made to minimize subjective opinion and to give the exact facts. The condition of all of the patients has been noted at the end of six months to make comparisons the more easy. All patients operated upon by the writer or his house surgeon in hospital and private practice, for real or suspected malignant disease, between April and October 1912, have been included in the list. The difficulty of keeping in touch with hospital patients is well known. By making almost monthly inquiry all of these, with few exceptions, have been followed.

It would take too much space to give abstracts of these individual records, so they have been grouped, and the results in the various groups will be noted.

OPERATIONS OF THE RADICAL TYPE. In the first group are included all operations in which the local growth, whether primary or recurrent, was apparently entirely removed. In a few cases the usual radical operation was somewhat modified, because of the strong probability that metastases existed beyond the operator's reach. Such patients undoubtedly have recurrences awaiting them even though they may not show for months. These are the patients for whom one wishes to obtain a quick recovery from operation by moderating the severity of the extreme radical type.

There are 27 operations in this radical group performed upon 25 patients, 2 of the patients having tumors on different parts of the body. There was no mortality from these operations.

There were 10 operations for epithelioma of the skin in various parts; 4 for epithelioma of the lower lip; 2 for epithelioma of the mouth; 6 for carcinoma of the breast; 1 for carcinoma of the uterus; 3 for sarcoma of the mouth; 1 for a recurrent sarcoma of the shoulder.

The condition of these patients at the end of six months as nearly as could be ascertained is as follows:

Examined and found without evidence of disease, 14; reported by letter to be free from disease, 3; have possible recurrence, 2; have certain recurrence, 1; died from recurrence, 2; passed from observation, 3; total number of patients, 25.

OPERATIONS FOR DIAGNOSIS. In the second group are placed 6 operations performed for diagnostic purposes in conditions of doubtful malignancy, although 4 of the patients had had previous operations. One patient had been twice operated on in other hospitals for cancer of the mouth. The removal of necrotic bone was followed by subsidence of symptoms, the condition probably being inflammatory. One patient came with recurrent ulcers of the forehead, which were excised and successfully skin-grafted. They were probably tuberculous. One patient had a swelling of the right hip nine years after removal of the right kidney for sarcoma. A lymph gland was removed and found normal. Tissue previously removed in another hospital by a deep incision into the hip had also been found to be normal. Examination with the x-rays was negative, yet malignancy must have existed, for the patient's pain and emaciation continued, and she died in about four months. The fourth patient had a leukoplakia of the tongue, a section of which was found to be merely papilloma. The fifth patient had a painful swelling of the posterior part of the lower jaw, variously diagnosed, and which was operated on three times before the swelling and pain and discharge disappeared. It was possibly an aberrant wisdom tooth. The sixth patient, married, aged thirty-six years, had a painless, fluctuating tumor of the breast for ten months. It was about one and one-half inches in diameter and contained purulent fluid. A section of its wall showed it to be inflammatory. All of these patients recovered promptly from the slight operations, the wounds of the second, third, and fourth healing primarily, and those of the others by granulation.

Their condition at the end of six months was as follows:

Well, no sign of cancer, 2; well, after another operation which failed to reveal cancer, 2; died, probably from undiscovered cancer, 1; passed from observation, 1; total, 6 cases.

OPERATIONS FOR SPECIAL OBJECTS. In the third group are included the operations performed for some special object upon patients whose apparent tumor or tumors could not be entirely removed. While the social and physical reasons for operation should both be considered in deciding for or against an operation, and in determining the nature of such operation, they so often coexist that it is quite impractical to separate these patients into two classes.

There was no operative mortality among the 24 patients of this group, as there ought not to be. One is justified perhaps in taking extreme risks in the attempt to accomplish a radical cure. There is not much excuse for sacrificing a patient's life in the attempt to give him temporary relief. While making all allowance for unknown weakness of a patient's organs, and unforeseen accidents during operation, it is still true that the operative mortality in this type of operating can be kept near the zero mark if the

surgeon carefully estimates the patient's power of resistance before operation and adheres to his resolve not to go beyond this point.

Ten of these patients had growths situated in or connected with the mouth. Only one of these was primary, the others were local recurrences, following one, two, or three operations. The object of operation in these cases was the removal of a painful or ulcerating tumor or to close a defect in the mouth. The periods of time through which such ends were accomplished and maintained, if expressed in months, would be 0, 1.5, 2, 2, 3, 4, 4, 5, 6, an average of not quite three months of comfort per patient. This is not the duration of life, but the period during which the patient could fairly be said to be in a distinctly better condition locally than before the operation. Five of the 10 patients died; 1 at two months from a more extensive operation performed elsewhere; 2 from recurrence in three months; and 2 from recurrence in four months. The remaining 5 were living at the end of six months, but, as stated above, only 1 of them was in a better condition than before his operation.

In 3 cases a recurrent tumor was situated in the antrum and orbit. One of these patients was in good condition for about four months. Then his pain recurred, and at the end of five months he was operated upon by another surgeon and died in three days. The other 2 patients received little or no benefit from operation, and both died in six weeks from extension of the disease.

In 2 cases recurrent tumors were situated in the neck and were very extensive. There was a partial removal in 1 case and an arterial ligation in the other. The first patient received very little benefit and died from an extension of the growth in less than two months. In the other case the deeper part of the growth seemed checked, but the superficial ulceration continued until it reached from ear to ear across the front of the neck. The patient was in good general health at the end of four months, but on account of the ulceration it is only fair to credit the operation with two months of improvement.

A recurrent epithelioma of the scalp, involving the skull, was widely excised, with the periosteum under the whole area of diseased scalp and a smaller portion of the skull. The wound granulated well, but the patient's headaches were not entirely relieved. In four months an additional amount of skull was removed, together with the dura mater, which the growth had penetrated. The patient again recovered promptly from operation, but headaches continued. He gained in health for a short time and then began to lose. At the end of six months he was somewhat anemic and had an almost constant pain. Three months of improvement is as much as can be credited to his first operation.

In one case of mixed-celled sarcoma in the parotid region, recur-

rent after two operations, a great mass of tumor tissue was removed, but it was found impossible to remove the growing edge of the tumor anywhere in the deeper portion. Consequently a rapid recurrence took place, so that although the wound healed primarily, local improvement could scarcely be said to have exceeded one month. The later history of this patient is unknown.

In 2 cases a painful recurrent breast tumor was removed from the wall of the chest and the wound covered with a flap of skin, taken in 1 case from the opposite breast. The wounds healed primarily, and the patients were in better local condition than before the operation, for periods of two months and four months respectively.

An extensive carcinoma of the vulva and groin was excised. Glandular involvement had already extended to the retroperitoneal and iliac and lumbar glands at the time of operation. Both wounds healed promptly, and although the external appearance was good for two months, pain and anemia progressed with scarcely any interruption, and the patient died in four months, with practically no benefit from operation.

A man with recurrent epithelioma of the perineum which extended into the deeper part of the pelvis beyond the ischium, too far for its safe removal, healed primarily and left the hospital entirely free from pain. In three months it was necessary to repeat the operation on account of a fresh recurrence, and this time the relief was of shorter duration. The patient wrote at the end of six months that at times he was suffering intensely. Two months is a fair estimate of the period of improvement attributable to the first operation in this case.

Two patients with extensive carcinoma of the uterus were treated by ligation of the internal iliac arteries. These patients had not been operated upon previously. In each case the abdominal wound healed primarily, and there was less hemorrhage and discharge than before the operation. Pain and emaciation continued in one case to such an extent that the operation had little more than a social value, although the patient was still able to get about at the end of six months. The other patient has been lost sight of.

One patient with extensive abdominal carcinoma was operated upon to satisfy the family. The growth was so widely disseminated that nothing could be removed. This patient died suddenly in about three weeks, possibly from embolism. There was no improvement from this operation.

The summary of these operations for special objects performed upon 24 patients shows:

Mortality from operation, 0; average period of improved health attributable to operation, two months; number of patients living at six months, 11; number of patients dying in less than six months, 11; number of patients lost sight of, 2.

An average gain of two months of improved health, may seem to some hardly worth striving for, but this is rarely the attitude of the patients. They are not only most grateful for any relief, but many of them take great pride in even temporary victory in a fight in which they know they must ultimately lose.

In conclusion it may be said that not every patient with a recurrence should be operated upon. There should be some special object to be obtained by such operation. The operation should be shaped to meet such special object, and should not be patterned after the radical operation. All patients who have been operated upon for cancer should be followed month by month, and single recurrences favorably situated should be promptly removed.

THERAPEUTIC ARTIFICIAL PNEUMOTHORAX.¹

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THE employment of pneumothorax, artificially induced, for therapeutic purposes was attempted at Loomis Sanatorium first in 1898, following the plan devised by Murphy. But few cases were so treated, however, and as the results were not such as to encourage a continuance of the method it was promptly abandoned. More recently the published reports of the satisfactory results attained by Forlanini, Brauer, Spengler, Saugman, and others in Europe, and Robinson and Floyd in this country, threw a much more encouraging light upon the procedure, and induced us to consider its readoption as a remedial measure in certain selected cases.

The beneficial effects of immobilization of an actively diseased lung as the result of a serous effusion into the pleura have long been recognized, and it has been our practice at Loomis Sanatorium not to aspirate in such cases unless pressure symptoms compelled us to do so, and then only to such an extent as would relieve the embarrassment, and to regard with satisfaction the occurrence of hydrothorax whenever it appeared on the affected side in the presence of an active and progressive lesion.

When it became apparent therefore that by means of an improved technique immobilization and compression of the diseased lung

¹ Presented in abstract at the Mid-winter Meeting of the American Sanatorium Association at the Montefiore Sanatorium, Bedford Hills, New York, December 7, 1912.

could be effected without serious danger to the patient, and with some promise of symptomatic relief, or even permanent benefit, in advanced and progressive cases, we determined to employ the procedure, but, for the time at least, to limit its employment to this unfortunate class and not to attempt it until the more conservative measures had failed. So far we have adhered to this practice, and have limited the treatment to such cases only as presented evidence of progressive disease in one lung and a comparatively slight lesion in the other, and where the prognosis has been unfavorable. This principle has governed our selection of cases for treatment at Loomis Sanatorium. For that matter, however, our rules for the selection of suitable cases are those generally followed.

A few enthusiastic advocates of the method have advised the procedure in early favorable cases, and have reported excellent results in such cases. But as the prognosis in this class is favorable for arrest under the ordinary dietetic hygienic treatment, the additional advantages of an artificially induced pneumothorax are questionable. The procedure is a radical one in any case, and while it is justifiable in those who have progressed unfavorably despite treatment by the ordinary methods, and in whom the prognosis is undoubtedly bad, we have felt that in the present state of our knowledge it should be limited to this class.

SELECTION OF CASES. Forlanini considers the following as indications for treatment by induced pneumothorax:

1. Uncomplicated unilateral phthisis, with slow or subacute course, and with a pleura free from adhesions, regardless of the degree of the lesion.
2. The same with such adhesions as may be removed by artificial pneumothorax.
3. Bilateral phthisis not running an acute course and with lesions on both sides not far advanced.

Claude Lillingston regards as favorable for treatment:

1. Cases of extensive and acute disease of one lung coupled with slight or no disease of the other lung.
2. Certain cases failing to respond to ordinary methods even with considerable disease of the better lung.²

Herbert Rhodes³ advocates the treatment in cases of

1. Pulmonary tuberculosis limited almost if not entirely to one lung.
2. Recurrent hemoptyses if at all severe.
3. Continued fever, cough, and general increase of disease on one side while the other lung is healing or only slightly affected.

Volhard,⁴ admitting that the first essential is the absence of large adhesions in the pleura, states that only an actual trial is

² *Lancet*, July 15, 1911.

⁴ *Munch. med. Woch.*, August 6, 1912.

³ *British Med. Jour.*, October 28, 1911.

capable of establishing the presence of such adhesions, and that physical signs and x-rays are of little value in determining this point. He considers that, so far as possible, the disease should be confined to one side though it may embrace the entire lung. The most suitable cases are those of unilateral cavities. Cases of "caseous pneumonia" are questionable. Severe hemoptyses may often be controlled. Abscess of the lung and miliary tuberculosis are not suitable. (Our experience in Case XII bears out this view with regard to abscess.) Severe cases of bronchiectasis are suitable, but require long continuance of treatment.

Klemperer⁵ in a paper on the subject advocates artificial pneumothorax in every case with continuous fever and much expectoration, when the condition is not too desperate, although he naturally considers unilateral cases most favorable. He does not advocate the procedure in early and otherwise favorable cases.

Almost all writers on the subject agree that slight or moderate laryngeal complications not only do not contraindicate the treatment, but are usually markedly benefited thereby, and a few report good results in tuberculous complications of the intestinal tract.

Robinson and Floyd,⁶ regard as most suitable for compression therapy such cases as present unilateral disease, but do not consider as contra-indications slight and comparatively inactive lesions on the opposite side.

With regard to first-stage cases, these authors argue—with what seems to us excellent judgment—that because in such cases pneumothorax *can* be readily established it is by no means proof that it *should* be, and that there is no reason to believe that pneumothorax therapy should be substituted when suitable institution or home treatment can be conducted.

Among the 102 cases reported by Brauer and Spengler⁷ many of the good results occurred in bilateral cases.

Paradoxical as it appears, notwithstanding the increased mobilization of the untreated lung improvement in the lesion on that side seems often to occur simultaneously with the improvement in the other lung, which is being treated by immobilization, although this does not always follow, as evidenced in Case VII of our series.

The most plausible explanation of this fact and that most generally accepted is that the improved condition and heightened resistance resulting from the reduced toxemia after successful compression place the patient in a much better condition for coping with the situation in the untreated lung.

In our series all of the tuberculous cases have been "far advanced" and bilateral, but in almost every instance the disease has been slight and comparatively inactive on the untreated side.

⁵ Berl. klin. Woch., December 18, 1911.

⁶ Arch. Int. Med., April 15, 1912.

⁷ Beitr. z. Klin. d. Tuberk., 1911, xxx.

TECHNIQUE AND APPARATUS. In none of our cases have we employed the open method of Brauer, although we realize that under certain conditions this method might be safer and more expedient, especially with beginners. But as we have so far met with no serious mishaps with the Forlanini puncture method, and as it is much easier to gain the patient's consent to this procedure, our experience is limited to this method.

When we decided to reintroduce artificial pneumothorax at Loomis Sanatorium we asked Doctor Cleaveland Floyd to come and demonstrate the technique and apparatus employed by Doctor Samuel Robinson and himself in their work.⁸ To this Doctor Floyd kindly consented, and the first injections were made by him in July, 1911. Five patients were selected as apparently suitable cases (Cases I, III, IV, XI, and XIII of our series). He brought with him the apparatus devised by Robinson, and Floyd needles, which he has modified from those used by Brauer, together with sufficient nitrogen for the first injections. Subsequently, and for several months until we were able to obtain a Robinson apparatus and the Floyd needles, we improvised a home-made apparatus with common aspirating needles, which answered the purpose, and as we were unable to obtain nitrogen at that time we used atmospheric air with apparently satisfactory results, except for the necessity of more frequent injections. From the start we have used a water manometer, which is very delicate and quite satisfactory except in cases with decided negative pressure, when it is sometimes awkward by reason of its delicacy.

Spengler employs a double manometer—one with a water column and the other with a mercury column, the latter to be used in cases with more pronounced negative pressure. This arrangement is obviously very convenient and time-saving.

In the selection of a site for the initial puncture we have been governed entirely by physical signs, avoiding proximity to cavity areas, as indicated by auscultation, and endeavoring to select a point where resonance on percussion and auscultatory signs indicate some respiratory activity and freedom from adhesions. In the main we have kept to the anterior and posterior axillary lines, but occasionally have made injection through the anterior chest wall as high as the fourth interspace and posteriorly to the angle of the scapula. The choice of site has been governed by convenience in each case. This settled the patient is given a hypodermic injection of morphine, $\frac{1}{16}$ to $\frac{1}{8}$ grain, and presently is placed upon the side opposite to that which is to be injected, with a pillow beneath to effect the greater separation of the ribs. The area selected for the puncture is painted with tincture of iodine. The parts are then

⁸ For description of this apparatus, see articles by Robinson and Floyd in *Trans. Amer. Clim. Assoc.*, 1911, and *Arch. Inter. Med.*, April 15, 1912.

anesthetized with a 1 per cent. solution of novocaine injected slowly—at first beneath the skin, then deeper, and finally a small amount into the pleural sac, when by the sensation of suddenly released resistance the point of the needle is believed to have passed the parietal pleura. It is seldom necessary to freeze the surface with ethyl-chloride, and patients very seldom complain of pain as the result of the introduction of the needle if a few minutes are allowed after the novocaine injection before proceeding.

We have customarily made a small incision through the skin with a sharp scalpel before introducing the pneumothorax needle, to avoid the pressure otherwise necessary to force the point of the large needle through the skin. The latter, with the stylet in place and the branch connecting with the manometer and nitrogen reservoir shut off by the valve-cock, is now introduced, preferably at a slight angle to avoid injuring the visceral pleura. The same sense of release of resistance, but more marked, that one notices in the preliminary injection of novocaine, generally indicates the puncture of the parietal pleura. The stylet is then withdrawn and the valve of the stylet tube closed. The branch valve is then cautiously opened and the movements in the water or mercury column in the manometer observed. The valve in the tube connecting with the nitrogen reservoir is, of course, closed. If the point of the needle in the pleural sac is not plugged and there are no extensive adhesions at this point, the manometer will indicate a more or less pronounced negative pressure with oscillations corresponding to the respiratory movements.

In the presence of extensive adhesions there will be little or no negative pressure or oscillations, while if the point of the needle has pierced the lung and is in communication with a bronchus there will be no sustained negative pressure, but oscillations may be quite as pronounced as when the point of the needle is in the pleura. Oscillations alone, therefore, do not necessarily indicate that one is between the pleural layers (see Case III).

F. Pielsticker and H. Vogt⁹ state that holding the breath by the patient readily shows on the manometer whether we are in the pleural sac or not. This does not appear to us to be a fact, however, for if the point of the needle is in communication with a bronchus and the patient holds his breath with the glottis closed a positive manometer reading may be registered just as it may when the point of the needle is between the pleural layers. In short, we have felt that a more or less pronounced negative pressure, with respiratory oscillations, are the only safe indications for the introduction of the gas.

When these indications are met we may safely assume that we are in the pleural sac. The manometer valve is then closed and the

gas allowed to pass into the chest. In the presence of a pronounced negative pressure this should be controlled by the valve, and permitted to run but slowly to avoid the shock of too rapid collapse of the lung.

The amount of nitrogen which may be safely injected at the initial puncture must, of course, depend upon the conditions in each case, but even when a negative pressure persists and no other contra-indications present, it is probably safer to limit the first injection to a few hundred cubic centimeters. Robinson and Floyd give as a maximum for the first injection 1000 c.c.

Bonniger¹⁰ believes that in a strong man 2000 c.c. and in a woman 1600 c.c. may be given at the first injection if manometer readings do not contraindicate. This seems to us unnecessarily heroic and not altogether devoid of embarrassing sequelæ if not of danger.

It is desirable, however, if possible to induce at the start a sufficient pneumothorax to give some symptomatic relief, either in lessened cough and expectoration or reduced fever, if for no other reason to encourage the patient more cheerfully to coöperate in subsequent treatment. But this can usually be accomplished by 500 c.c. or 600 c.c., and such an amount rarely gives any sense of discomfort to the patient. In most cases, without extensive adhesions limiting the amount of the initial injection to this figure, there will still be a negative pressure at the end of the injection.

Subsequent injections had best be made at intervals of not more than a few days until the manometer readings are neutral or slightly positive, and the x-rays show as complete a lung compression as is possible. After this is accomplished the intervals between the injections are governed by symptoms—especially the amount and character of the sputum, temperature, etc., and the x-rays. If atmospheric air is used the intervals will necessarily be shorter than when nitrogen is employed.

More or less effusion occurs in about one-third of the published cases, and according to some of the German writers has an inhibitory influence upon the gas absorption. This has seemed to be a fact in our experience.

The amount of gas injected after the initial operation is determined by the manometer readings and the feelings and condition of the patient. We have thought it neither necessary nor advisable to secure a marked positive intrathoracic pressure, and have been content with a neutral or very slightly positive manometer reading at the conclusion of the injection. Even this sometimes gives a sense of "tightness" and slight temporary discomfort, especially during the early stages of treatment.

The manometer is the key to the whole situation, and is the one device which has made artificial pneumothorax practicable as a

¹⁰ Berl. klin. Woch., August 26, 1912.

therapeutic measure. The other accessories to the operation are more or less a matter of convenience. One may improvise an apparatus using a plain trocar or aspirating needle, and employ atmospheric air in place of nitrogen if necessity or expediency compel, but a manometer is an essential to the success of the treatment.

The accidents which may occur in the process of inducing pneumothorax are fully described in the literature. The principal ones are pleural reflex, gas embolism, and surgical emphysema. With care and a little experience in the method they are for the most part avoidable, but when they do occur they are somewhat disconcerting.

In our experience we have met a mild "pleural reflex," pleural "eclampsia" (Forlanini) once (Case IV). Robinson and Floyd believe that novocaine anesthesia of the pleural membranes obviates the risk of this complication, and Rhodes states that if the nitrogen is warmed "pleural reflex" is impossible. In our case novocaine was not employed and the atmospheric air which we were using at the time was not warmed. It is possible therefore that one or both omissions were responsible.

It does not seem to us that air embolism is a serious menace if reasonable care is exercised and the behavior of the manometer is understood and closely watched. In our early experience, when on one occasion we injected air into the lung, which escaped through a bronchus (Case III), we made the mistake of relying upon the manometer oscillations in the absence of negative pressure, but had our needle point been in a bloodvessel there would have been no oscillations and we should not have proceeded.

We have met with a mild and unimportant surgical emphysema about the point of puncture several times, with little or no consequent inconvenience. A more serious matter was that of Case X, when by reason of adhesions the nitrogen made its escape along the trachea and into the subcutaneous tissue of the face, neck, and chest on the side opposite to that injected, causing for a time a disconcerting dyspnea through involvement of the submucous tissue in the larynx.

In the 16 cases here reported we have included 6 which proved inoperable by reason of adhesions. For statistical purposes these should be excluded, but we have included them because they have seemed to us in some respects instructive. We have classified our cases on a basis of results attained, and they are not arranged in sequence as to point of time.

Of the 10 operable cases, as is shown in the summary, 2 have shown marked and apparently permanent improvement; 7 have shown temporary improvement and more or less symptomatic relief, while in 1 case of lung abscess no improvement was observable. As has been stated our cases have all been far advanced,

active, and bilateral, with decidedly unfavorable prognoses, a fact which should be borne in mind when considering the results attained.

Since October, 1912, we have been controlling the injections by means of the *x*-rays. Some of these plates are reproduced.

We look upon the method with more confidence as we proceed and in our later cases—too recently placed under treatment to justify report at this time—we feel encouraged to hope for better results than it is possible to report in the present series. In any case there is no small satisfaction in the consciousness that we possess a means by which we can offer another chance of life, slender though it may be, to this forlorn class of otherwise hopeless invalids.

CASE I.—J. P. C., male, aged twenty-two years. Admitted April 15, 1911. Condition: far advanced. Turban iii (R iii—L i). Duration of disease: since September, 1910 (ten months).

Symptoms. Since admission in April has had persistent hectic fever (98° to 99° in A.M., 101° to 104° in P.M. Pulse, 100 to 120. No normal days since admission).¹¹ Cough: expectoration averaged from 140 to 190 grams per day. Continued loss of weight; 4.15 kg. since admission. Patient on absolute rest in bed.

Physical Signs. Extensive involvement of whole right lung, with excavation of most of the upper lobe. Slight infiltration scattered throughout left lung, mostly at root. On account of extensive rapidly progressing destructive lesions and of severe constitutional disturbance this case was regarded as almost hopeless—in fact, practically moribund.

July 30. First injection of 750 c.c. of nitrogen without difficulty. Evidently slight if any adhesions. Marked immediate improvement; temperature falling to normal on the following day and remaining there subsequently. Expectoration dropped from 160 on the day of operation to 65 grams on two succeeding days, then rose again to from 120 to 160 grams.

August 8 to September 14. Three injections of air, each of about 1000 c.c. Marked continued improvement.

October 15. Signs of fluid have replaced pneumothorax signs in right chest. Injections therefore discontinued.

January 18, 1913. Up to the present date patient has made steady improvement. He is now walking three or four hours a day, and his weight has increased from 42.75 kg. at time of first injection to 63.52 kg., a gain of 20.77 kg. (45 pounds). The expectoration still remains rather high, averaging about 90 grams a day. Tubercle bacilli have been very few since establishment of pneumothorax, never more than No. V (Gaffky scale), and sputum examinations sometimes have been negative for several months in succession.

¹¹ In this article all temperatures are recorded from rectal observations.

Physical examination and x-ray plate indicate a markedly fibroid contracted right lung with pleural thickening, and a resultant retraction of chest walls, diaphragm, and heart. Left side clear (see Fig. 1).



FIG. 1.—Case I. November 23, 1912. Shows marked contraction of right lung with resulting contraction of chest walls, diaphragm, and heart. Densely infiltrated upper lobe. Slight infiltration at left apex and root.

Summary. Satisfactory result in a progressive and seemingly hopeless case, the beginning of improvement following immediately on injection of pleural cavity.

CASE II.—A. A. N., male, aged nineteen years. Admitted September 5, 1912. Condition: far advanced. Turban iii (R iii-L i). Duration: since spring of 1912.

Symptoms. Periods of slight fever, expectoration averaging 50 grams a day. At rest in bed.

Physical Signs. Indicate active infiltration throughout most of right lung; most marked in upper lobe. Slight inactive infiltration in left upper lobe.

October 16. First injection of 800 c.c. nitrogen without difficulty. Pressure still negative at end. Temperature, which had been 100° or slightly over every afternoon, on second day after operation became normal and remained there.

October 22. 700 c.c. injected. Continued normal temperature; expectoration falling steadily. Patient was started on five minutes' walking, twice a day, gradually increased.



FIG. 2.—Case II. November 12, 1912. Shows pneumothorax occupying right chest, upper lobe of lung collapsed, middle and lower lobes partially collapsed. Probable diaphragmatic adhesions preventing complete collapse of lower lobe.

January 18. Injections have been continued until present at intervals of one to three weeks, from 500 c.c. to 700 c.c. each time. Improvement has continued uninterrupted. Patient is on manual labor squad, working three or four hours a day. Expectoration only 2 to 4 grams a day. Continued weight gain (see Fig. 2).

Summary. Very satisfactory result. Arrest of activity and continued improvement following institution of pneumothorax.

CASE III.—J. H. D., male, aged forty-four years. Admitted June 6, 1911. Condition: far advanced. Turban iii (R iii—L i). Duration of disease: since 1901 (ten years).

Symptoms. Remittent fever, 99° to 101° most of the time since admission. Pulse, 68 to 90. Cough; expectoration averaging 172 grams in June and 128 grams in July, the month previous to first injection. Patient at rest in bed.

Physical Signs. Indicate extensive long-standing involvement of the right lung, with probable cavity in the upper lobe; much less marked infiltration in the upper lobe of the left lung.

Complication. Slight grade of nephritis, without enlargement of heart. Rather persistent extrasystole of heart beat, occurring usually about every six beats.

July 30. First injection of 700 c.c. of nitrogen in the right pleural sac. Apparently no adhesions. Following the injection sputum weight fell slightly for a few days, from 145 to 106 grams., then rose to 150 grams again. No change in fever.

August 8 to September 2. Four injections of air from 1000 to 2000 c.c. each made. Some improvement in condition shown by normal temperature and lower sputum weight (70 grams per day).

September 19. An attempt was made at injection, in several places, but impossible to get manometer reading showing needle in pleural sac. Needle probably entered lung, as on the following day there was about a dram of blood in sputum. Physical examination showed dulness in the lower part of the right chest, with very deficient breath sounds. Expectoration, however, remained at comparatively low figure, and exercise was gradually increased to thirty minutes, twice a day. Had also gained about 4.5 kg. of weight.

October 27. Another attempt was made at injection. Oscillations obtained on manometer, but no negative pressure. Needle was supposedly in pleural sac, and 2000 c.c. of air were injected. No change in manometer reading, and no evidence from physical signs of any resulting pneumothorax. Therefore conclusion was reached that the point of the needle must have passed through the adherent pleura into the lung, and that injected air passed out through the bronchi. Further attempts at injection were abandoned.

Patient's condition continued about the same until February, 1912, when severe hemoptysis occurred. After this his condition became gradually worse until discharged from the Sanatorium, May 24.

Summary. Temporary improvement followed injections. This case illustrates the danger of allowing too long a time to intervene between injections, unless condition of compression of lung is carefully controlled by physical examination or better by x-ray plates. Undoubtedly between the injections of September 2 and the attempt at injection on September 19, an interval of seventeen days, the air had become absorbed and the pleural surfaces adherent.

This case illustrates also the inadvisability of proceeding with

the injections in the absence of negative pressure, as shown by the manometer even in the presence of characteristic oscillations.

CASE IV.—M. J. T., male, aged thirty-two years. Admitted November 6, 1910. Condition: far advanced. Turban iii (R iii-L i). Duration of disease: since 1906 (five years). Chest examination indicates: Right, extensive infiltration throughout lung, with excavation in upper lobe. Left, compensatory changes, with probably small areas of infiltration, principally at root.

Symptoms. Fever, remittent (98° to 101°); cough; expectoration averaging over 100 grams a day. Patient at rest in bed.

Complication. Toxic nephritis.

July 30, 1911. First injection of 750 c.c. nitrogen into right chest. Following this there was no special change noted in symptoms, except slight decrease in expectoration.

August 8. 650 c.c. of air. Patient very nervous during operation, and in condition verging on collapse immediately following. Results of this injection appeared to be a further slight decrease in expectoration and a lower temperature range.

August 16. 400 c.c. of air. Severe collapse following operation, with rapid feeble pulse and loss of consciousness ("pleural reflex"). For this reason further injections were discontinued.

August 25, nine days after operation, temperature became lower and remained practically normal except for occasional days (never reaching, however, 101°). Expectoration also less for several days after injection, running from 60 to 120 grams, but amount gradually increasing after discontinuance of injections.

September 15. Severe hemoptysis, followed by death.

Summary. Slight temporary improvement in condition following injections. Probably a case of "pleural reflex."

CASE V.—I. J. A., female, aged twenty-four years. Admitted September 21, 1910. Condition: far advanced. Turban iii (R iii-L ii). Duration of disease: since March, 1910.

Symptoms. Almost constant daily remittent fever during the year following admission. Temperature usually between 101° and 102° in the afternoon. Night sweats. Loss of weight, 10 kg. (22 pounds) since admission. Expectoration averaging between 150 and 200 grams daily. In bed or sometimes sitting up in a chair for a few hours, since admission, except for a few days in December, 1910, when, during a period of temporary improvement, temperature was normal and she was allowed ten minutes walk, twice a day. No normal days since that time.

Physical Signs. The physical signs indicate extensive involvement of the right lung, with probable excavation in upper lobe. Compensatory and probably some fibroid changes in left lung.

November 13, 1911. First injection of 700 c.c. air into right pleural sac. Expectoration fell from 220 grams on day before injection.

tion to 105 grams on following day, remaining low for several days. No marked effect on fever.

November 16 to December 22. Eight injections of from 600 c.c. to 900 c.c. each, given at intervals of from three to seven days. Temperature now normal, and expectoration only 80 to 100 grams a day.

March 6. Injections continued at intervals of one to two weeks up to this time, condition remaining about the same, except for some tendency to increase of expectoration. Following the injection on this date the temperature gradually rose and fever was present, usually about 102° in the afternoon for the following month. Expectoration averaged about 150 grams. For a few days in the early part of April temperature was normal, but then rose again, and fever remained until discharged from the Sanatorium on May 4, 1912. No further injection given during this time. At time of discharge examination showed signs of pneumothorax throughout the right chest except at the apex, and slight amount of fluid at base.

Summary. This case was distinctly disappointing in results. A practically unilateral case, with high expectoration and probable cavity, it seemed to offer good indications for pneumothorax. But in spite of the fact that the latter was successfully established, and that the lung was apparently well collapsed, no permanent good results followed. Probably the temporary improvement in condition shown by reduction or absence of fever and lower expectoration may be attributed to the pneumothorax, but this improvement was only transitory. (Subsequent to discharge patient went to Saranac Lake, where pneumothorax has been maintained with apparently good results. At last report, December 1, 1912, patient had gained over twenty pounds, and has been feeling much better.)

CASE VI.—F. S. M., male, aged forty-five years. Admitted January 5, 1910. Condition: far advanced. Turban iii (R iii—L i). Duration: since May, 1909.

Symptoms. Patient's condition for first nine months after admission in January, 1910, was steadily progressive. Short periods of fever, heavy expectoration, and loss of weight continued until patient, although six feet two inches in height, in October, 1910, weighed only 46.05 kg. (101 pounds). Unexpectedly and without any decided change in treatment he at this time began to improve, this improvement continuing most spectacularly until in June, 1911, he had reached a weight of 73.3 kg. (161 pounds, 60 pounds gain) and was on two hours' exercise a day. The expectoration did not decrease materially, however, during this time, remaining most of the time over 100 grams a day. In the fall of 1911, the patient began to lose ground again. At the time of the first injection, January 30, 1912, he weighed 65.5 kg. (144 pounds), was without fever, and had an expectoration of 171 grams a day.

Physical signs at the time of injection indicated an extensive involvement of right lung with probable excavation in upper lobe. Compensatory signs in left lung, with slight infiltration of upper lobe.

January 30. First injection of 400 c.c. of air. Pronounced negative pressure was obtained and marked respiratory oscillations, indicating absence of pleural adhesions.

February 1. Two days later 1000 c.c. of air was injected, the pressure still being slightly negative at the end of the injection. Patient complained of no inconvenience except a slight feeling of tightness through chest.

February 7 to March 25. Four injections of about 1000 c.c. each.

During this time the patient had gained a little weight (650 grams) and felt perhaps somewhat better, but the chief effect of the injection had been on the amount of the expectoration, which had fallen from 171 grams to 103 grams per day. The signs indicated an extensive pneumothorax throughout lower two-thirds of right chest. The signs continuing it was not thought necessary to repeat the injections until April 23 when 1300 c.c. of nitrogen was injected.

During May the expectoration fell to 65 grams, by far the lowest that it had been at any time since his admission. He was, however, losing weight again at this time.

June 14 to July 20. Three injections of 600, 950, and 1200 c.c.

During June and July, although there was a complete collapse of the lung, the condition did not improve, there being a continual loss of weight, and the expectoration rising again from 65 to 117 grams.

No further injections were made until September 7, the pneumothorax signs continuing.

September 7. Attempt made at injection, but most surprisingly it was found impossible to obtain a negative pressure or to get good respiratory excursions; 250 c.c. of nitrogen were cautiously injected, but it was deemed inadvisable to attempt more than this.

September 9. Another attempt at injection was made, with the same result. No negative pressure could be obtained, and only 100 c.c. nitrogen were injected.

No further injections have been attempted. The explanation of the failure to obtain a satisfactory negative pressure was not clear.

An examination on September 21 showed that in addition to the pneumothorax there was also a small amount of fluid in the right chest. These signs are still present (see Fig. 3).

The patient's condition is slowly growing worse. The expectoration has risen again to 151 grams, and the loss of weight has continued.

Summary. Temporary improvement. Disappointing case in that so complete a collapse did not give better and more lasting improvement.



FIG. 3.—Case VI. November 12, 1912. Hydropneumothorax of right chest with collapse of right lung.

CASE VII.—J. D., male, aged forty-two years. Admitted October 1, 1911. Condition: far advanced. Turban iii. Duration of disease: since March, 1911.

Symptoms. Constant fever since admission, averaging about 98° in A.M. and 102° in P.M. Expectoration, 70 to 80 grams a day. In bed since admission.

Complications. Laryngitis of mild grade. Dry otitis media. Diabetes mellitus of mild grade. On carbohydrate restricted diet the urine had become and remained free of sugar.

Physical Signs. Indicate extensive involvement of left lung, with cavity signs in lower part of upper lobe. Slight infiltration of apex of right lung.

Case did not seem an especially favorable one for pneumothorax treatment in view of the complications and the advanced condition.

December 8. First injection of 300 c.c. air into the left chest. Temperature, which had reached 101° and over every day since admission, on the day following pneumothorax, reached only 100.4° , rising again, however, on the succeeding days.

December 12, 1911 to January 2, 1912. Four injections of from 600 to 1000 c.c. each. Marked improvement in condition. Temperature normal and expectoration less. Patient now sitting up two or three hours a day.

January 5. Graduated exercise (walking) begun and gradually increased to fifteen minutes, twice a day. This was followed, however, by a return of fever to about 101° in the afternoon.

January 17. 600 c.c. of air. Temperature again normal on following day, but immediate return of fever when exercise was resumed.

January 30. 700 c.c. of air. Temperature again fell to slightly over 100° on the following three days, although after that it rose again to 101° or over, even though no further attempts at exercise were made. Expectoration fell to an average of about 50 grams.

February 7. 700 c.c. of air. No improvement followed this injection. A few days later there was a marked exacerbation of fever, as high as 103° on most days, the expectoration rose and the general condition grew progressively worse. Although the signs of extensive disease and cavity in the left lung had at this time been replaced by the pneumothorax signs, yet on the right or "good" side there were signs of a considerable exacerbation of the disease, and this was held to be the reason for the increase of symptoms. Under these circumstances it was not deemed advisable to continue further injections. The patient's condition grew progressively worse from this time on and death occurred on May 27. The pneumothorax signs in the left chest continued until the end, although becoming much less extensive than immediately after the injections. During the last few weeks before death dyspnea was a very marked and distressing feature.

Summary. Considering the condition of the patient at the time when the injections were first made, the improvement which followed, even though only temporary, was rather remarkable. The ultimate exacerbation of the disease on the "good" side may perhaps have been due to the increased compensatory activity of that side occasioned by the pneumothorax, though there is no real evidence leading to such a conclusion aside from the old *post ergo propter* argument. Even if so it is the only case in which we have seen any exacerbation of the disease that could be attributed, even remotely, to the pneumothorax, and we feel that the contingency is so remote a one that it may be reasonably disregarded in properly selected cases.

CASE VIII.—R. F., male, aged eighteen years. Former Sanatorium patient, resident of Liberty. Condition: far advanced. Turban iii (R i—L iii). Duration of disease: since 1908 (three years).

Symptoms. Severe continued hemoptysis over period of several days. Disease rather rapidly progressing since previous summer. Temperature and pulse normal.

Physical Signs. The physical signs indicate extensive involvement of the left lung, with numerous bubbling rales. No signs of moisture on the right. Thorough examination was not made at the time of injection on account of hemoptysis.

Pneumothorax was attempted on this patient as a means of checking the hemorrhage. As the left lung had been the one chiefly affected at the time of his residence in the Sanatorium, and as a superficial examination at the time of the injection showed the evidence of abundant moisture in the left lung, it was assumed that this was the seat of the bleeding.

November 27. First injection. Puncture was made in the seventh interspace of the left axilla. Novocaine anesthesia; 150 c.c. of air injected. Only slight negative pressure at the start, and last part of air injected under positive pressure. Complained of severe tearing pains in lower left chest during the injection.

December 1 (three days later). No hemorrhage since injection until the night of November 30, when there was a small hemorrhage during the night and a second at 11 A.M. today. Slight surgical emphysema about previous puncture site. 250 c.c. of air injected. No local anesthetic used. Most of the injection was made under positive pressure. Patient complained of severe pain in the left shoulder during and following the operation, lasting for several hours. Severe enough to cause attacks of syncope.

December 4. Patient's condition improved. No more hemorrhages, except slightly blood-streaked sputum. 300 c.c. of air injected, last 100 c.c. under positive pressure. Some pain in shoulder again caused.

December 7. No further hemorrhage. General condition seems slightly better; 150 c.c. of air injected, again causing severe pain. As there were no further hemorrhages, and the injections caused such severe pain, and as it seemed impossible on account of pleural adhesions to establish any extensive pneumothorax, further injections were not attempted.

Four months after the injection the patient died. Autopsy showed an extensive fibroid infiltration and a tuberculous bronchopneumonia of the left lung, and the pleura everywhere tightly adherent. No trace could be found of the pneumothorax, even in the area directly under the point where the puncture had been made. Evidently after the absorption of the air the pleural surfaces became adherent.

Summary. This case aside from the apparent control of the hemorrhages by the pneumothorax, is interesting in several particulars. There were evidently extensive pleural adhesions (a fact afterward established at autopsy), preventing any extensive collapse. The air, most of it forced in under positive pressure, must have broken up enough of these adhesions to form a pocket. This was probably the cause of the tearing pains felt in the lower chest on the first injection. In connection with the pains felt in the left shoulder during and subsequent to the injection most interesting is the work of J. A. Capps, of Chicago.¹² In several cases of pleural effusion, using a trocar through which a long blunt wire was passed, he investigated the pain sense by touching various parts of the pleura. When the arch of the diaphragm was touched pain was usually felt in the neck, at some spot, the position varying in different subjects, along the ridge of the trapezius muscle. In this case of pneumothorax under discussion the pain was referred to the upper part of the shoulder, a position nearly corresponding with that in some of Capp's subjects. It seems likely therefore that this is a correct explanation of his pain, that it was a referred pain due to a pulling on the arch of the diaphragm by pleuritic adhesions.

CASE IX.—D. H., female, aged thirty years. Admitted January 27, 1912. Far advanced. Turban iii (R iii—L i). Duration of disease: since 1899 (thirteen years).

Symptoms. Fever (averaging 101° in p.m.), night sweats, gastric disturbance, expectoration (60 grams a day).

Complications. Toxic nephritis; laryngitis, with ulceration.

Physical Signs. Scattered infiltration throughout the right lung, most marked in the lower lobe. Slight changes in left upper lobe. Litten's sign present on both sides, more marked on left.

March 9. First injection of 300 c.c. of nitrogen into right side; pressure becoming neutral at this point. Evidently adhesions preventing further collapse. Temperature and expectoration both somewhat lower on succeeding days.

March 18 to April 23. Four injections of about 300 c.c. each.

Injections were discontinued after this, as there was no very noticeable result.

The physical signs when the injections were discontinued indicated a pneumothorax occupying lower right chest up to the first rib in front, and just above angle of scapula posteriorly. At present date (December, 1912) these signs have entirely disappeared. An x-ray plate also shows no remaining pneumothorax.

Summary. The patient did improve somewhat during the six weeks that injections were given, but as this improvement had

¹² An Experimental Study of the Pain Sense in the Pleural Membranes, *Archiv. Int. Med.*, December, 1911.

apparently begun before the first injection, and has continued since they were stopped, it is doubtful whether the pneumothorax was an important element in the improvement, especially as no very complete collapse was obtained.

CASE X.—C. C. S., male, aged twenty-seven years. Admitted July 20, 1911. Condition: far advanced. Turban iii (R ii - L ii). Duration of disease: since August, 1910.

Symptoms. Constitutional symptoms not marked. Patient taking walking exercise up to two hours a day. Expectoration of about 100 grams a day. Improvement on ordinary hygienic dietetic treatment, had apparently reached a standstill.

Complication. Tuberculous laryngitis without ulceration.

Physical Signs. These indicated an extensive involvement of the left lung, with cavity signs in upper lobe, the base being comparatively clear. Litten's sign-present. Signs of slight impairment of right lung anteriorly, with no definite signs of disease posteriorly. Apparently a favorable case for pneumothorax treatment.

January 25, 1912. First injection of 500 c.c. of air. Rather difficult to enter the pleural cavity with needle. Oscillations finally obtained on manometer, but with only slight negative pressure. The air was forced in under moderate positive pressure.

On the night following the injection the patient felt a severe pain in chest. Soon after this the neck began to swell and there was some difficulty in breathing. Examination showed surgical emphysema of the subcutaneous tissues of neck and face, and extending down on right chest wall. No emphysema about the puncture point. Emphysema cleared up in a few days.

The probable explanation of this condition is that there were pleural adhesions preventing a collapse of the lung, which also explains the failure to obtain a negative reading of the manometer. The 500 c.c. of air, forced in among the pleural adhesions under positive pressure, must have burrowed its way to the mediastinal region and there broken through the pleura into the mediastinum, whence it found its way, following the course of the trachea and large vessels, into the neck, spreading from there into the face and over the chest wall.

Summary. Unsatisfactory case on account of pleural adhesions. This case illustrates well one of the dangers of attempting to inject gas when there is not a negative pressure as revealed by the manometer. Oscillations on the manometer are not enough, in view of this experience, to justify injection. There must also be a definite negative pressure.

CASE XI.—A. S. H., male, aged thirty-eight years. Admitted April 9, 1910. Condition: far advanced. Turban iii (R iii - L ii). Duration of disease: since 1896 (fifteen years).

Symptoms. Severe cough and expectoration, averaging 220 grams a day the month previous to first injection. Slight afternoon temperature (100.4° to 100.8°). Patient at rest sitting up in a chair during the day and riding to meals.

Physical Signs. Extensive infiltration throughout the right lung, most marked in lower lobe. Possible small effusion at base (probably proved by result of injection, however, to be thickened pleura). Compensatory changes, in left lung. No present signs of activity in this lung, but probably scattered old lesions.

On account of extensive changes in the lower lobe the case did not seem an especially favorable one for pneumothorax.

July 30, 1911. First injection of 250 c.c. of nitrogen into the right pleura. Impracticable to inject more on account of positive pressure. Pleura found to be very thick. No change in condition noted.

August 8. Several attempts made to enter pleura in various localities, but impossible to obtain negative pressure on manometer.

On account of evident thickened adherent pleura, further attempts at pneumothorax were discontinued.

Summary. No improvement. Unsatisfactory case for treatment on account of pleural adhesions.

CASE XII.—A. M. P., male, aged thirty-one years. Admitted July 17, 1912. Condition: non-tuberculous case. Abscess of left lung. Duration: since February, 1912.

Symptoms. Periods of fever and night sweats, hemoptyses, expectoration varying in amount from 100 to 500 grams a day; loss of weight, 10 kg. (22 pounds).

Complications. Infection of sphenoidal sinus. Part of the expectoration is undoubtedly from this source.

Physical Signs. Slightly impaired resonance and modified breath sounds at the right apex, without rales. On the left, marked dullness, feeble breath sounds to the third interspace in front and middle of the scapula behind. Occasional rales over this area anteriorly.

Repeated search by concentration methods of examining sputum has failed to show bacilli. The von Pirquet is also negative. Case diagnosed as lung abscess and diagnosis confirmed by Doctor T. C. Janeway.

November 13. First injection of 500 c.c. of nitrogen into the left chest.

November 16. 600 c.c. injected.

November 23. 600 c.c. injected.

Expectoration has been slightly decreased following these injections. Running between 450 and 500 grams before, and now about 350 grams. Occasional hemoptyses and attacks of fever still continue (see Fig. 4).

December 12. Patient discharged. Condition: progressively less favorable. Expectoration as high as 500 grams.

December 29. Patient died at Presbyterian Hospital, New York. Autopsy showed lung abscess.

Summary. No improvement following collapse of lung in case of lung abscess.



FIG. 4.—Case XII. November 15, 1912. Pneumothorax occupying lower part of left chest. Lung partially compressed. Dense shadow of lung abscess extending out from hilus.

CASE XIII.—C. G., male, aged twenty-two years. Admitted February 26, 1911. Condition: far advanced. Turban iii (R i - L ii). Duration of disease: since November, 1909 (one year and nine months).

Symptoms. Excellent constitutional condition. Cough and expectoration (average 60 grams).

Physical Signs. Left lung: Extensive infiltration throughout, with probable small cavity anteriorly between third and fifth ribs. Right lung: Slight infiltration in upper lobe and at root.

Complications. Tuberculous laryngitis. Case appeared to be an excellent one for artificial pneumothorax.

July 30, 1911. First injection. Artificial pneumothorax attempted. Pleural cavity entered and negative pressure obtained. As soon as gas began to enter, patient complained of severe tearing pains in chest, becoming unbearable; therefore only 75 c.c. could be injected. As patient was not at all of neurotic temperament, these pains were thought to indicate pleural adhesions.

August 30. Second attempt at injection made, with same result. Further attempt therefore discontinued.

Summary. Inoperable case on account of pleural adhesions.

CASE XIV.—R. H. H., male, aged forty-five years. Admitted October 30, 1911. Condition: far advanced. Turban iii (R iii — L i). Duration of disease: since February, 1909.

Symptoms. Previous to admission to the Sanatorium had had attacks of pleurisy on right side, at one time with effusion. Expectoration about 50 grams a day. No marked constitutional symptoms except loss of weight.

Physical Signs. Extensive fibroid changes in right lung, with probable dry cavity in upper lobe, widespread adhesions at base, marked compensatory changes in left lung. Litten's sign absent on right side.

First injection, July 12, 1912.

The case did not seem very promising for pneumothorax treatment on account of the evidence of adhesions at the right base. On attempting to perform the operation this diagnosis was confirmed, it being found impossible to obtain manometer readings indicating an entrance of needle into pleural sac.

Summary. Inoperable case on account of pleural adhesions.

CASE XV.—C. N. N., female, aged thirty-one years. Admitted December 28, 1911. Condition: far advanced. Turban iii (R iii — L i). Duration: since 1905 (seven years).

Symptoms. Cough, expectoration (128 grams) fever (about 101° in P.M.), progressive loss of weight. Several attacks of pleurisy at onset of disease in 1905.

Complications. Laryngitis without ulceration. Probable tuberculosis of lower intestinal tract. Mild grade of nephritis.

Physical Signs. Physical signs indicate infiltration throughout right lung with probable cavity in upper lobe, few infiltration areas in left lung.

April 2, 1912. First injection. Attempt at pneumothorax. Satisfactory negative pressure not obtained. Slight respiratory oscillations; 100 c.c. of nitrogen cautiously injected.

April 6. Second attempt made, with no better result. Only 75 c.c. injected. Evidently extensive pleural adhesions.

Summary. Inoperable case on account of pleural adhesions.

CASE XVI.—J. C. W., female, aged forty-three years. Admitted August 2, 1907. Condition: far advanced. Turban iii (R iii — L i). Duration of disease: since 1899 (thirteen years).

Symptoms. Patient entered the Sanatorium in August, 1907, five years ago, in advanced condition, with high fever and expectoration. Had fever almost every day for two years. Since then the constitutional condition has improved remarkably, and for the past three years she has been, for most of the time, free of fever. Gain of weight of 17 kg. (37 pounds). Expectoration always high, about 120 grams during month previous to injection. Exercising about one-half hour, twice a day.

Physical Signs. Effusion on the right side at time of admission in 1907. Signs at time of injection indicated extensive fibroid infiltration throughout right lung, with destructive changes in upper lobe and thickened pleura and possibly some effusion below. Areas of infiltration and compensatory hypertrophy in left lung. Considered a rather unfavorable case before injection on account of probable pleural adhesions.

July 18, 1912. Attempt made at injection, but needle evidently entered thick pleural adhesions. No negative pressure or oscillations of manometer obtained. No gas injected.

Summary. Inoperable case on account of thickened adherent pleura.

General Summary. In 16 cases in which the treatment has been tried 2 have shown marked and apparently permanent improvement, 6 have shown temporary or slight improvement, in 1 case hemorrhages have apparently been controlled, in 1 case of lung abscess no improvement followed, while in 6 cases, on account of pleural adhesions, either no gas could be injected or not enough to produce any sufficient collapse.

THE DIAGNOSIS OF TUBERCULOSIS OF THE KIDNEY.¹

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It is only within comparatively recent years that tuberculosis of the kidney has become recognized as a distinct pathological entity amenable to treatment offering excellent chances for cure. While formerly looked upon as merely a terminal manifestation

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of a general tuberculous infection or as a rare disease difficult to diagnosticate, modern methods of examination, together with an accurate knowledge of its mode of infection, pathology, and clinical course, have proved quite the reverse to be true.

Without going into a discussion of the possible avenues of invasion, we can say that it is now a generally accepted fact that the tubercle bacilli reach the kidney by way of the blood stream, and that this infection is primarily unilateral in the great majority of cases. Probably because of the intimate vascular connection a specific infection of the opposite kidney originates more frequently from its sister organ than from any other focus in the body. The course of the disease is progressive, passing from bad to worse, and, according to Israel, there is no authentic case on record which has been cured by other than surgical measures.

While primary tuberculous cystitis must be considered a pathological rarity, the bladder is commonly the seat of disease secondary to a renal infection. In the presence of a tuberculous cystitis, with its changes promoting incomplete evacuation as well as stenosis of the orifice of the sound ureter, an ascending infection of the second kidney, with the ureter as the avenue of entry, is likely to follow, as the experimental work of both Albarran and Baumgarten has demonstrated. Starting as a single or multiple focus of infection the further progress of the disease may produce changes altering not only the pathological but the clinical picture as well. Excluding miliary tuberculosis, which is merely the local manifestation of a general miliary tuberculosis, four types may be differentiated. Following an eruption of tubercles scattered more or less diffusely throughout the kidney, there may be little or no tendency to caseation, but rather to connective-tissue proliferation, transforming the kidney into a dense, irregular mass, at times impossible to differentiate from a neoplasm. Should areas of softening be present they frequently are surrounded by firm fibrous tissue impregnated with lime salts. The fibrous as well as the fatty capsule participates in this general tissue proliferation. A second type much rarer than the others is characterized by ulceration of the renal papillæ, so-called tuberculous papillitis which was first described by Israel, and due, in his opinion, to the passage of the bacilli through the tubules of the kidney, lodging at the papillæ, where they exert their destructive action. The type most commonly encountered is that presenting one or more cavities at the junction of the cortex and medulla, and not infrequently located at one or the other poles. These cavities vary in size, and may or may not communicate with the pelvis of the kidney. There is generally a chronic interstitial nephritis affecting the remainder of the renal parenchyma. In all these types, especially during the earlier stages of development, the kidney may present no gross enlargement; on the contrary, when extensive interstitial changes with fibrosis

are present the kidney may be smaller than normal. It is important to remember that the enlarged kidney may be the healthy one, the increase being due to compensatory hypertrophy incident to the added work which it must assume when the function of the opposite side is seriously impaired. The terminal stage of these various forms is seen in the tuberculous pyonephrosis, with almost or quite complete destruction of the renal parenchyma; a mixed infection may be engrafted on the tuberculous, transforming the kidney into an enormous pus sac. The ureter and bladder likewise participate in the tuberculous process, the infection being secondary to the primary renal focus, and of urogenic origin in most instances. Primary tuberculosis of the bladder is so rarely seen that its demonstration in the female sex means almost invariably that we have to deal with a primary focus in one or both kidneys. Changes in the ureter may be entirely absent, but, as a rule, some evidences of the tuberculous infection are to be found. These may consist merely of discrete tubercles scattered here and there along the mucous membrane, or, in cases of longer standing, there may be extensive thickening of the ureteral walls, with ulceration, connective-tissue proliferation, and contraction, forming one or more strictures which may completely occlude the ureter, resulting in the closed pyonephrosis. While this is but a cursory review of the pathology of tuberculosis of the kidney it represents the chief manifestations found clinically.

In spite of an enormous amount of literature and discussion on this subject, the diagnosis of renal tuberculosis is seldom made or even suspected by the general practitioner. The obsolete term irritable or nervous bladder remains a favorite expression of ignorance, dividing honors equally with false conceptions concerning the importance of uterine deviations in regard to the production of vesical irritability. An uncomplicated retroflexion seldom if ever produces urinary symptoms, and in the light of our present knowledge, acquired largely through the extensive use of the cystoscope, the term nervous bladder should be stricken from medical nomenclature. As a safe working rule, proven only by the rare exception, every bladder presenting symptoms should be considered the site of some organic lesion, and no effort should be spared to determine the exact nature of this lesion. We do not mean to imply that every irritable bladder is the seat of tuberculosis, but we do claim that only by following this rule can we hope to make the diagnosis sufficiently early to permit the application of proper surgical treatment.

We have reviewed the histories of twenty-five cases of tuberculosis of the kidney which have been admitted to Dr. Clark's service in the University Hospital, and the symptomatology which we shall give represents largely the summary of these cases.

In studying these histories, one is immediately impressed by

the rarity with which the symptoms are directly referable to the kidney itself; even in cases of enormous pyonephrosis or complete occlusion of the ureter the most the patient may experience is a dull, indefinite aching sensation in the lumbar region, and even this may be entirely absent. On the other hand, the pain may be so severe as to warrant the diagnosis of calculus; these acute attacks of colic may be due to sudden obstruction of the ureter by a thick plug of pus or may be associated with an extensive perinephritis, and especially periureteritis, upon which is engrafted an acute congestion following exposure to cold or at the time of the menstrual period. This pain is doubtless due to two factors, namely, increased tension upon the thickened, inelastic capsule of the kidney and partial or complete occlusion of the ureter incident to the swelling induced by increased vascularity.

The first and by far the most prominent symptoms of renal tuberculosis during the entire course of the disease are those referable to some abnormality in the function of the bladder. Starting, as a rule, with painless polyuria all degrees of dysuria are met, including the most intense strangury and even complete incontinence. Such vesical disturbances are not necessarily due to an organic lesion of the bladder itself; even in the earliest stages of renal involvement, with no extension of the process beyond the renal parenchyma, the vesical irritability may be intense. This is difficult to explain, but is supposed to be of reflex origin, due to the intimate nerve connections between the kidney, ureter, and bladder or to the irritating action of toxins eliminated in the urine. In our series of cases there were only two in whom some evidences of bladder involvement were not present, and in both there was increased frequency of urination but no dysuria. As a rule, by the time the patient presents herself for examination the bladder has become involved and the urinary disturbances are in more or less direct proportion to the degree of extension. These symptoms may be decidedly intermittent in their severity, with intervals of comparative comfort between the acute exacerbations. It is doubtless true that many cases reported as improved under tuberculin treatment are merely manifestations of the natural course of the disease.

In addition to these local symptoms are those commonly present in any chronic infection. While in the early stages the general health is but little if any affected, sooner or later indefinite gastrointestinal symptoms, especially nausea and vomiting, present themselves. There is a progressive loss in weight, and the patient tires easily on slight exertion. Contrary to the opinion so commonly expressed the temperature is normal, or at most shows only a slight evening elevation. Irregular fever, with chills and sweats, are evidences of a mixed infection or a more generally disseminated tuberculous process.

With the exception of the earliest cases, limited to a small abscess in the renal cortex, some degree of pyuria is the rule. The quantity of pus will naturally vary with the extent of involvement of the urinary tract; the greater the bladder involvement the greater the pyuria. In the presence of a mixed infection the urine is often loaded with pus, while in even advanced cases of pure tuberculous infection the pus is found in comparatively small amounts, may be entirely absent, or may be abundant at one examination, with only a moderate amount at the next. These variations are easily explained when we refer to the pathology. In the early cases there is no connection whatever between the tuberculous focus and the pelvis of the kidney. Or in the more advanced case, where we are dealing with a closed pyonephrosis, there is no communication with the bladder, and the pus cannot escape. The rapid change in the quantity of pus is more or less characteristic of renal tuberculosis, and is due either to the rupture of a cortical abscess into the pelvis of the kidney or to some factor promoting better drainage of an abscess which already communicates with the pelvis. While the discussion of the bacterial content of the urine is not in our province, we may be permitted to state the general working rule that pyuria without demonstrable bacteria, either by smear or culture, strongly suggests the possibility of a tubercular infection. Macroscopic hematuria is rarely seen even in the advanced stages of renal tuberculosis, and when present is usually of vesical rather than renal origin. In one form of the disease—namely, the tuberculous papillitis—profuse hematuria is characteristic. Albuminuria is usually present, but small in amount compared to the degree of renal involvement.

The objective findings must of necessity depend upon the type of disease as well as upon the degree to which the infection has extended to the bladder and ureter. In the early cases, in which the disease is limited to the renal cortex, physical examination will show no abnormalities whatever; usually, however, an enlargement of the kidney is manifest. Under normal conditions the right kidney can be palpated in 75 per cent. of women, consequently disease on this side is more easily demonstrated than when the left kidney is involved. Even a considerable enlargement on the left side may escape detection; this is especially true in those cases in which perinephritic thickening anchors the kidney in its high position. While the kidney may be diminished in size in the sclerotic type of the disease, this is rarely demonstrable clinically; the kidney either escapes detection entirely or a fixed mass can be palpated, consisting not only of kidney but its infiltrated fatty capsule. It must be remembered that a demonstrable enlargement does not necessarily indicate the diseased side, since this increase in size may be due to compensatory hypertrophy of the sound kidney. Tenderness, especially at the costovertebral angle, is

rarely absent, and is directly proportionate to the extent of perinephritis. When the disease has extended down the ureter there may be tenderness along its course, but even in those cases with marked thickening and complete stenosis we have never been able to say definitely that the ureter could be palpated by abdominal examination. Thickening of the vaginal portion of the ureter can be readily palpated, and its demonstration may be of importance in determining the side affected. While many authors lay great stress upon this point, and some even go so far as to state that it is pathognomonic of tuberculosis, too great dependence upon its significance will lead one astray, for we have been able to demonstrate ureteral thickening in several cases of pyelocystitis in which tuberculosis could be absolutely ruled out. Its presence is suggestive, but by no means characteristic.

The tuberculin reaction is of doubtful value; we have employed only the subcutaneous injection, and its results were considered significant only in the presence of increased kidney or bladder symptoms.

Lastly and by far the most important factor in the diagnosis is the cystoscope. It is often the only means at our command to determine the nature of the infection, and only by its use can we estimate the extent of involvement of the urinary tract, which is of the most vital importance in its bearing upon the advisability of surgical intervention. In women the diagnosis of vesical tuberculosis means almost invariably that the primary focus is in one or both kidneys; while in the majority of cases the changes in the bladder are characteristic, we occasionally meet instances of renal involvement, with a normal bladder picture, or, on the contrary, there may be such extensive disease of the bladder that the typical lesions of tuberculosis are masked. In the former the cystoscope is still a valuable aid in that it determines definitely the source of the pyuria; further, in the presence of vesical symptoms, with insufficient evidence in the bladder or its surrounding organs to account for these symptoms, tuberculosis of the kidney is a strong possibility. While simple cystoscopy may not suffice in the far-advanced changes to warrant a diagnosis of tuberculosis, it at least shows that we are dealing with a severe infection which demands more detailed examinations to determine its exact nature. These include microscopic and bacteriological studies of the urine, ureteral catheterization, and one or more of the functional kidney tests. In referring to the pathological changes in the bladder we follow the classification of Caspar, designating them as tuberculosis of the bladder and tuberculous cystitis; the former is a distinctly localized process, the latter general, involving not only the mucosa but often the muscularis as well. At the beginning of the disease the bladder as a whole shows little or no change from the normal; the characteristic picture is presented at the ureteral orifice and the mucosa surround-

ing it. Due to ureteral thickening the orifice is no longer linear but round, with edema, reddening, and superficial, irregular ulceration of its edges and adjacent mucosa. Further ulceration transforms the ureteral ostium into a large, crater-like opening, with rigid, unyielding walls covered with indolent granulation tissue. Contraction of the scar tissue of the ureter produces not only marked irregularity of the orifice, but actual retraction of the entire ureteral region, so that this portion of the bladder assumes a funnel-shape, with the larger opening directed downward. The orifice may also be surrounded by the so-called edema bullosum, or the picture may closely resemble a neoplasm when papillary alterations are present. Miliary tubercles are likewise found, usually situated in the trigone, but may be located in the fundus or sides of the bladder. In our series of cases tubercles were found only twice, which leads us to the conclusion that they are rather unusual manifestations. With further extension of the disease or in the presence of a mixed infection, which is so often present in the advanced cases, a more or less general cystitis ensues, with irregular ulcers and ecchymoses scattered here and there over the universally inflamed mucosa. Because of its long duration the infection involves not only the mucosa but extends into the musculature, thereby diminishing the size of the bladder until its capacity may be reduced to a few centimeters. Under these circumstances the ureteral orifices may be completely obscured and the typical pathology so masked that a diagnosis of tuberculosis is possible only by animal inoculation.

Having determined the nature of the infection, it is of equal importance to ascertain whether one or both kidneys are involved. In our opinion this can be accomplished only by catheterization of the supposedly sound side with a careful chemical, microscopic, and bacteriological study of the collected urine; a normal ureteral orifice does not prove that the corresponding kidney is not diseased, since the infection may not have extended beyond its original renal focus, nor is a normal functional test sufficient because the disease may not involve enough of the renal parenchyma to seriously interfere with its working capacity. Theoretically, catheterization of the sound ureter is objectionable because of the danger of promoting an ascending infection from an already diseased bladder; practically, however, this objection does not hold when care is exercised in passing the catheter directly into the ureter without touching the mucosa of the bladder and inserting the catheter only a few centimeters rather than into the pelvis of the kidney. The diagnosis is not complete until we have demonstrated not only anatomical but also functional integrity of the opposite kidney; the fact that the patient is free from the symptoms of renal insufficiency is certainly of the greatest value, but this must be further substantiated by the employment of one or more of the functional

tests. For this purpose we prefer indigocarmine, not only because of its simplicity and adaptability in even the most extensive forms of bladder infection, but also, and what is even more important, it affords a reliable index of the relative functional capacity of the sound kidney.

When these various examinations have failed to reveal the site of disease, the skiagraph may offer valuable information, as was our experience in one case which baffled the diagnosis by every other means. The cortical abscesses may cast a shadow when a deposit of lime salts is also present, but this is unusual, and therefore of but little practical importance. By means of ureteral catheterization and the injection of collargol the skiagraph may reveal not only strictures of the ureter, but also one or more cortical abscesses in communication with the pelvis of the kidney. In the one case referred to the small abscess was clearly shown and proved at operation.

This *resume* includes the more important clinical factors concerned in the diagnosis of tuberculosis of the kidney. While in many cases the diagnosis is plainly evident from the clinical findings, in others the nature of the infection is obscure and can be recognized only with the assistance of the laboratory. This phase of the subject will be covered by Dr. Laird.

The diagnosis of renal tuberculosis in the female is practically determined by positive tuberculous findings in guinea-pigs inoculated with the urinary sediment. In the male, however, the close relationship between the urinary and genital tracts renders the differentiation of the two, as the possible source of infection, necessary, and this lies principally in the clinical field. If by the clinical methods already described the kidneys have been proven normal, a thorough examination of the genital tract should be made to determine a possible involvement of the epididymides, vasa deferentia, seminal vesicles, prostate, or testes. As the kidneys are usually the primary foci of infection in the urinary tract, so the epididymides are the primary source of tuberculous infection in the genital tract. Primary tuberculous prostatitis, seminal vesiculitis, and orchitis have been reported, but these conditions were probably due to an indeterminate focus in the epididymis. As such foci may be clinically indeterminable, the secondary involvement of the other genital organs is naturally of importance in the diagnosis. The physical examination may reveal an enlarged, non-tender, non-painful, hard, nodular epididymis; thickening and induration of the vas deferens; a slightly nodular, non-tender, markedly indurated, and fixed prostate or seminal vesicle. The symptoms of tuberculosis of the genital tract are referable to disturbance of the genital function—namely, sexual erethism, discomfort or pain on ejaculation (which may, in acute cases, be slightly bloody), general weakness and nervousness after intercourse, leading finally to neuras-

thenia, usually sterility and later impotence. Pus may be absent from the urine in incipient cases of tuberculous epididymitis, but is usually present in cases with secondary involvement. The chronicity of the process is an important diagnostic point. The final diagnosis depends upon the finding of the tubercle bacilli in the seminal fluid or prostatic secretion.

LABORATORY METHOD.—Until the last few years the laboratory diagnosis of renal tuberculosis has depended upon the intraperitoneal or subcutaneous method of inoculation of rabbits or guinea-pigs. These methods consume about six weeks time or the time required for general tuberculosis to develop in the inoculated animals. To save this valuable time, Bloch, in 1907, advocated the inguinal method of inoculation, which requires only ten days for a positive diagnosis. Much has already been written upon this subject, but the advantage of the Bloch method as a time-saver over the old method, and the fact that the older, slower method is still quite generally used, especially in this country, were thought sufficient reasons for touching upon it once more in this comparative study.

The technique is as follows: A twenty-four hour specimen of urine is collected from the suspected case in a large sterile bottle, without the addition of a preservative. About 10 c.c. of urine from the lower portion of the specimen are placed into each of two centrifuge tubes and centrifugalized for from two to four hours, dependent upon the speed of the centrifuge, when the supernatant urine may be poured off, leaving the sediment in the bottom of the tubes.

From the sediment in one of the tubes, slide smears are made, which are then fixed, stained and examined microscopically for pus, blood, and bacteria, especially acid-fast bacilli. (Gabbett's method of staining the tubercle bacilli was employed in this work.) Pus is nearly always present in the urine in renal tuberculosis, varying greatly in amount, not only in the various stages of the disease, but also from time to time even in the late stages. This pus has, moreover, often a characteristic appearance both macroscopically and microscopically. The pus in tuberculous urine is grayish and granular, giving the urine when held to the light a ground-glass appearance in contrast to the soft yellowish appearance given by the pus in other conditions. The presence of blood, although occasional in renal tuberculosis, is more indicative of other pathological conditions of the genito-urinary tract. Acid-fast bacilli are nearly always present in the sediment in renal tuberculosis, but are frequently seen in the non-tuberculous conditions. The differentiation of the tubercle bacillus from the other acid-fast organisms, in spite of unceasing efforts at differential staining, is microscopically impossible. Although here as macroscopically the appearance of the pus and the bacilli is

sufficiently characteristic to arouse a suspicion which will afterward be proven a surety in a large percentage of cases. In contrast to the more or less discrete leukocytes comprising the pus seen in non-tuberculous genito-urinary affections, there are present large clumps of degenerated leukocytes, about the periphery of which will be found the typical slender, slightly curved, beaded rods, arranged in semiparallel groups, and giving one the impression that these organisms had a distinct part in bringing about the degeneration, whereas the other acid-fast organisms appear to have been accidentally dropped into a field of pus cells. The final diagnosis, therefore, must always depend upon animal inoculation.

For this purpose a suspension of the sediment in the second tube is prepared by shaking with 5 c.c. of sterile water. Two healthy, normal guinea-pigs are inoculated. The inguinal glands of the pigs are first slightly injured and thus rendered more susceptible to the attack of the tubercle bacillus, by pressing and rolling them between the forefinger and thumb for a few moments prior to the inoculation. $2\frac{1}{2}$ c.c. of the prepared suspension, unheated, are then injected into each of the two pigs, subcutaneously, in the inguinal region directly below the glands. Pressure is again applied for a short time and repeated on the two days following the injection.

Ten days after the inoculation one of the two pigs is chloroformed and the inguinal glands on the injected side removed. These may be either sectioned, stained, and examined for tubercle bacilli, or, more simply and quite as reliably, finely macerated and pressed out between two microscopic slides, and fixed, stained and examined immediately.

In the majority of positive cases the microscopic examination of the inguinal glands results in the discovery of the tubercle bacilli in a few minutes. In some cases, however, in which the tubercle bacilli have been probably few in number or of low virulence the resultant inguinal involvement is so slight that the bacilli may escape detection by a cursory examination, and therefore a thorough search of every portion of the inguinal tissue should be made before a negative diagnosis is given.

In order to control the Bloch method of inoculation the second pig was allowed to live the required six weeks and then examined for general tuberculosis.

STATISTIC TABLE.

	Positive.	Negative.	Doubtful.
Clinical diagnosis	22	29	7
Bloch method	17	40	1
Subcutaneous method	17	40	1
Total, 58 cases. Positive by laboratory methods, 77.3 per cent.			

There were 58 cases of suspected renal tuberculosis examined by the combined clinical, Bloch, and subcutaneous laboratory

methods. Twenty-two cases were proven, 7 by operation and 15 by subsequent clinical course, to have tuberculosis of the genito-urinary tract; 29 were proven, 3 by operation and 26 by subsequent clinical course, to be non-tuberculous; 7 cases were still clinically doubtful. By the Bloch method of inoculation, 17 cases were positive, 40 negative, and 1 doubtful, due to the premature death of the pig. By the subcutaneous method 17 were positive, 40 negative, and 1 doubtful, due to the same cause. In the clinically proven cases of tuberculosis, therefore, 77.3 per cent were positive by both laboratory methods. The 7 clinically doubtful cases gave negative results by both methods. Of the clinically proven negative cases all but 1 gave negative results, and this was positive by both the Bloch and subcutaneous methods. This case was brought to operation on account of the positive laboratory findings; the apparently affected kidney was exposed and split, and showed, macroscopically, an interstitial nephritis and no evidence of tuberculous involvement. Two of the proven positive cases which gave negative laboratory results were closed cases, the ureter of the affected side being obstructed: 1 had advanced bilateral renal involvement, which shortly caused death; the other 2 were frank cases of unilateral renal tuberculosis. There were 2 clinically positive cases, each giving negative results by each of the two laboratory methods and positive by the other. Another positive case showed numerous tubercle bacilli in the inguinal glands of the pig at the expiration of ten days, and only one small focus of infection in the spleen of the other pig at the end of six weeks.

NOTE.—The Oppenheim method of hepatic inoculation was tried in a few instances resulting in every instance in the premature death of the pigs from septicemia.

CONCLUSIONS.—1. The kidney is the primary site of disease in tuberculosis of the female urinary tract; as a rule the infection originates from a focus in some other organ and gains entrance to the kidney by way of the blood stream.

2. The pathology varies greatly in kind as well as in degree, but a definite type usually predominates, altering both the pathological and clinical pictures.

3. Subjective symptoms referable to the kidney disease are by no means characteristic; they are often entirely lacking, may be expressed by a dull, aching sensation in the lumbar region or by attacks of colic resembling calculus.

4. The most prominent symptoms are those referable to deranged bladder function; starting with painless polyuria, all degrees of dysuria are met, including the most intense strangury and even incontinence. These symptoms may be decidedly intermittent in their severity, with intervals of comparative comfort. A cystitis which does not readily yield to the usual appropriate measures should arouse the suspicion of renal tuberculosis.

5. Some degree of pyuria is the rule; hematuria the exception. Intermittent pyuria suggests tuberculosis of the kidney. Pyuria without demonstrable bacteria by smear or culture in a catheterized specimen is likewise suggestive. Albuminuria is usually present, but small in amount compared to the degree of renal involvement.

6. In the absence of mixed infection the temperature is normal or shows only a slight evening elevation; irregular fever with chills and sweats is evidence of a mixed infection or a more generally disseminated tuberculous process.

7. The palpatory findings are dependent upon the type and extent of the pathological changes. While enlargement of the diseased kidney is usually manifest, it is important to remember that compensatory hypertrophy of the kidney may be given erroneous conclusions in determining the diseased organ. Thickening of the vaginal portion of the ureter is of value in diagnosis, but by no means characteristic of tuberculous infection.

8. The tuberculin reaction is of doubtful value; the subcutaneous injection should be employed and its results are significant only in the presence of increased kidney or bladder symptoms.

9. By far the most important agent in determining the diagnosis is the cystoscope, which in the majority of cases shows a picture so characteristic that the nature of the infection is at once recognized. Only by its use can we decide the extent of disease as well as the condition of the opposite kidney as regards both its anatomical and functional integrity.

10. The diagnosis of renal tuberculosis should be made in every suspected case by the combined clinical and laboratory examination.

11. The Bloch method of inoculation of guinea-pigs should be used, because it is equal in reliability to the older method, and the diagnosis may be made in at least 77.3 per cent. of cases in ten days compared to six weeks by the subcutaneous or intra-peritoneal methods, which should also be used as controls.

12. A positive laboratory result by either method determines the diagnosis of tuberculosis of the genito-urinary tract; of renal tuberculosis in the female, the exact focus in the male to be determined by additional clinical and laboratory means.

13. A single negative laboratory result, regardless of thoroughness of examination, does not determine an absolute negative diagnosis of renal tuberculosis, as the manifestation of this disease is essentially intermittent. Negative results obtained in three successive weekly examinations should, however, bear considerable weight in the diagnosis.

INVAGINATION OF MECKEL'S DIVERTICULUM ASSOCIATED
WITH INTUSSUSCEPTION: REPORT OF A CASE,
WITH A STUDY OF RECORDED CASES.

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MECKEL'S diverticulum has long been known as a cause of abdominal disorders. A common source of disturbance is obstruction caused by the constriction of coils of intestine about the diverticulum when both its ends are attached. When the distal end is free the diverticulum itself not uncommonly becomes in some manner twisted upon itself or strangulated.

A less common source of trouble is inversion of the diverticulum into the lumen of the bowel, thereby causing obstruction to the intestine. In a number of instances inverted diverticula are associated with intussusception of the intestine. The diverticulum may pass into an intussusception without itself becoming inverted. Which of these events is cause and which effect is a matter of controversy that will later receive attention. It is the purpose of this paper to collect all the cases of inversion combined with intussusception recorded in the literature. We are able to add one of our own. On the basis of the data thus collected the question of pathogenesis will be discussed, the problem of the pathology stated, the results of treatment as heretofore carried out summarized, and the problem of the best method of treatment presented for the critical consideration of the reader. Our case is as follows:

F. M. W., aged nineteen years. Two years ago the patient had a severe attack of abdominal cramps. He attributed it to eating raisins. The attending physician at his first visit found nothing, but an examination made a day later revealed a tumor immediately below the umbilicus. This was supposed by his physician to be a mass of raisins and he manipulated it with his fingers in order to break up the lump. The cramps subsided and flatus and stool passed on the next day. The patient was free from any complaint from that time until December 18, 1912, when he became chilly and nauseated while loading a wagon. The two days following he felt much improved. On the third day he ate a hearty breakfast and later a ham sandwich, and took a small drink of whisky, to which he was not accustomed. He immediately began to have cramp and walked about to lessen the pain. After a few hours he vomited freely. The pains increased during the afternoon, and he rolled about from pain, and a doctor was summoned. Morphine was administered hypodermically and was repeated the following day.

Many enemas were employed during the following days, but pain and vomiting continued. During this period the physician was able to palpate a tumor to the right of the median line. On Friday the enema brought away a piece of the meat eaten on the Sunday previous; this gave some relief, and a little supper was eaten. On the following day he became worse again and was brought to the Halstead Hospital Saturday afternoon, with the diagnosis of intestinal obstruction. On examination the abdomen was but little sensitive, and there was no rigidity. Two hypodermics of morphin had been given during the day, which made this negative evidence of little value. There was moderate distention; no dulness in either flank; the tongue was dry and coated; there was no evidence of impending collapse. Pulse, 144; temperature, 97°; respiration, 24.

The abdomen was opened in the median line below the umbilicus. When the peritoneum was opened about a quart of straw-colored fluid escaped. The intestinal coils appearing in the incision were injected and much distended. There was no paralysis. The ileocecal portion of the intestine was at once sought and was found lying over the kidney. It presented a tumor. When the tumor was drawn into the wound it was seen to be an intussusception through the ileocecal valve, about twelve inches long, with a distinct tumor at its upper extremity. The tumor was thought to be a polyp which had produced the inversion of the gut. When the intussusception was reduced by traction and pressure on the tumor a dimple remained over the base of the supposed polyp. This made it obvious that the tumor mass was an inverted Meckel's diverticulum, with a thickened apex. By careful pressure the diverticulum was restored to its former position. The diverticulum was nearly the diameter of the gut from which it sprang, and was about two and a half inches long. The mass in its apex was about the size of a hulled walnut. The diverticulum was clamped just below the solid mass and a mattress suture passed on the ileal side of the clamp. The clamp was removed and the gut severed, the edge being cauterized with carbolic acid and iodine. This raw end was then inverted into the lumen of the gut. The contracture of the walls of the intestine after the suture line had been inverted resulted in narrowing the lumen of the gut more than had been intended. No evil resulted, however, as the lumen remaining was the size of a finger, but looked small in contrast to the adjoining dilated gut. The cecum was replaced and the loop of ileum containing the stump of the diverticulum was pulled over above and distal to the cecum. An inch stab opening was made in the side just above the crest of the ilium. A small, flat gauze pack was placed over the ileum and a drainage-tube below it. The incision in the median line was closed completely.

Following the operation the patient awoke quickly, and at 6 P.M.

his chart showed pulse, 132; temperature, 100.8°; respiration, 28. At 9 P.M.: pulse, 124; temperature, 101°; respiration, 28. He attempted to vomit and his stomach was emptied by lavage of a large amount of greenish fluid. Flatus was expelled late in the evening following an enema. There were emesis and repeated gastric lavages in the days following. On Tuesday, the third day, there was free bowel movement, with much flatus, and the patient complained of hunger. On the fifth day, Friday, the chart showed pulse, 92; temperature, 99.2°; respiration, 24. Saturday: pulse, 78; temperature, 99.4°; respiration, 24; on the seventh day: pulse, 68; temperature, 98.4°; respiration, 20. During the first two days there was a profuse drainage of cloudy serum from the drainage opening; this became reduced at the end of the second day, and the drains were removed. The skin of the entire central incision opened on the sixth day, and a considerable amount of pus was expelled.

Pathologic examination of the specimen: The part removed consisted of a mass about the size of a hulled walnut, with a flange of diverticular wall below it in which the muscular and mucous coats could be readily made out. On section the mass was seen to be composed in part of blood clot, giving the appearance of a submucous accumulation of blood of some days' duration. At the apex of the tumor immediately beneath the peritoneum was a cap 3 or 4 mm. thick, which was pearly white and resembled when cut the section of a skin papilloma. Microscopic examination showed the submucous thickening was due to an old blood clot. Toward the opening of the diverticulum the mucosa was normal, but at the apex it was continuous with the white thickened cap. The latter proved to be composed of glandular tissue arranged in two distinct layers; an inner, made up of Brunner's glands somewhat irregularly disposed; and an outer, which resembled the benign adenomas so often found in the intestines. This arrangement suggested strongly the aberrant masses of pancreatic tissue, which have often been reported present in Meckel's diverticula, and particularly the case in which Küttner observed both Brunner's glands and aberrant pancreatic tissue. The fact that in our case some of the misshapen Brunner's glands terminated in the adenomatous portion, raises the question whether the so-called pancreatic tissue may not in reality have been aberrant intestinal glands. The cases in the literature are, however, given with too little detail to permit one to do more than speculate in this direction.

The cases which we have been able to find reported in the literature as invagination of a Meckel's diverticulum with intussusception are some of them so incomplete as to be mere statements that such cases were observed. The reports of others show that they do not belong to the group of cases under consideration. A third group is reported fully enough to permit a judgment of the anatomic char-

acters of the lesion and to give a picture of the clinical course. The last group only will receive detailed consideration, though a list of the incompletely reported cases will be appended.

Case 1.—1894. Studsgaard, *Centralbl. f. Chirurgie*, 1894, xxi, 934.

Male, aged thirty-seven years. At operation there was found peritonitis and invagination of the bowel, the latter containing an introverted Meckel's diverticulum. A section of intestine was removed and death followed the same day.

Case 2.—1898. De Quervain, *Centralbl. f. Chirurgie*, 1898, xxv, 839.

Male, aged sixteen years. Patient was seized with severe abdominal pain and vomiting, without known cause. There were numerous borborygmi, but no passage of gas. No blood in stool. There was palpable resistance in the ileocecal region, but no tumor. Moderate distention and diffuse tenderness. Laparotomy revealed a gangrenous intussusception, which was removed entirely and an artificial anus produced. Death followed in a few hours. The part removed contained an invaginated Meckel's diverticulum 5 cm. long.

Case 3.—1898. v. Stubenrauch, *Centralbl. f. Chirurgie*, 1898, xxv, 137.

Female, aged five and a half years. Patient became acutely ill with severe colic and tenesmus, with bloody stools. On second day she had vomiting. On the fifth day she was admitted in a collapsed condition. The abdomen was moderately distended, sensitive to pressure, and especially prominent below the navel. At operation an intussusception of the ileum was found, 10 cm. from the ileocecal valve. Resection; death in two hours. The intussusception was gangrenous and contained an invaginated Meckel's diverticulum $5\frac{1}{2}$ cm. long.

Case 4.—1898. Erdmann, *Ann. Surg.*, 1900, xxxi, 186; *New York Med. Jour.*, April 16, 1898.

Male, aged nine years. Illness began with colicky pains in right side of abdomen, then vomiting and bloody stool. The next day tenesmus, and on the second day severe shock and a palpable tumor extending from the right iliac fossa to the tenth costal cartilage. The abdomen was distended, tympanitic, and tender. At operation an intussusception was found with its apex within six inches of the ileocecal valve. It was irreducible, gangrenous, the intestines were deeply engorged, and there was a quantity of pus in the abdominal cavity. Resection, end-to-end anastomosis; death in four days. At the end of the invagination there was an introverted Meckel's diverticulum.

Case 5.—1898. Moroni, *Virchow's Hirsch Jahresbericht*, 1898, xxi, 289. Male, aged twenty-six years. Onset acute; pain and vomiting. Had previous operation for ileus due to axial torsion.

Renewed obstruction, death. Pathology, a complete ileal intussusception caused by inversion of Meckel's diverticulum, which contained a fibrous polyp the size of a cherry.

Case 6.—1899. Strauch, *Zeitschr. f. klin. Med.*, 1899, xxxviii, 465; *Hildebrandt's Jahresbericht*, 1899, v, 627.

Female, aged six years. Had been subject to severe attacks of colic for years. Suddenly had complete obstruction and was operated after thirty-six hours. There was an invagination of the intestine 15 cm. long, the apex of which consisted of a Meckel's diverticulum completely invaginated; resection; death.

Case 7.—1899. Robinson, *British Med. Jour.*, 1899, ii, 1416.

Male, aged five years. Patient had pains in belly, which became localized about the umbilicus during the night, and were accompanied by bilious vomiting. There were hiccough and thirst, but no distention. The next afternoon the pain became continuous, and distention appeared and became worse in the evening. There was a little blood in the enema fluid. There was no rigidity nor special tenderness. There was a lump over Poupart's ligament, which was comparatively dull on percussion, and on palpation by rectum there was a cylindrical mass three inches long in Douglas' pouch. Upon incision clear fluid escaped. The main invagination was easily reduced, but the introverted Meckel's diverticulum had to be excised. The patient collapsed and died in two hours after the operation.

Case 8.—1899. Brunner, *Beitr. z. klin. Chir.*, 1899, xxv, 344.

Male, aged four years. There had been no previous illness. The onset was sudden, with abdominal pain. In a few hours there was a bowel movement, followed by considerable hemorrhage, after which the pain became continuous, and the constipation absolute, notwithstanding frequent enemas. The abdomen was distended, but not rigid. There was dulness on percussion, from the right iliac fossa to the region above the pubes, and in the latter situation a hard nodular mass could be felt. Operation was performed three days after the beginning of the illness. An invagination of the ileum extending into the cecum was found, which, being irreducible, was resected. The operation lasted two and a half hours. The patient recovered. Within the invagination was an inverted Meckel's diverticulum, with a tumor at its apex. The tumor lay immediately beneath the serosa, unattached to the intestinal wall, and was formed of two parts, a superficial layer of fat and a deeper portion, which was glandular, resembling the pancreas.

Case 9.—1900. Bayer, *Centrallbl. f. Chirurgie*, 1900, xxvii, 1138.

Male, aged two and a half years. Illness began with a bowel movement attended by severe pain, which was followed by obstruction. A tumor was palpable in the ileocecal region, and later in the region of the hepatic flexure. At operation the bowel was disinvaginated without difficulty. There became apparent a

dimple, 15 cm. from the valve, which marked the base of a Meckel's diverticulum 3 cm. long, which was invaginated into the lumen of the gut. This was everted and its lumen obliterated by a series of puckering stitches; recovery.

Case 10.—1900. Hohlbeck, *Arch. f. klin. Chir.*, 1900, lxi, 1.

Male, aged eighteen years. Abdomen somewhat distended, but not tender. Vomiting of yellow fluid. The flanks were dull on percussion. No tumor was palpable until the patient was in narcosis, when a lump was found in the ileocecal region. At operation an ileocecal invagination was found and easily reduced. A Meckel's diverticulum was present, and had been drawn into the intussusception. The mucosa was separated from the muscle of the diverticulum and was invaginated, forming a floating tumor as large as a walnut in the lumen of the bowel. The diverticulum was excised. Death on the second day.

Case 11.—1901. Eve, *British Med. Jour.*, 1901, ii, 582.

Male, aged thirteen years. Illness began twenty-eight days before operation. Upon incision an intestinal invagination appeared and was resected. The patient died. At the apex of the intussusception was an invaginated Meckel's diverticulum.

Case 12.—1901. Pitts, *British Med. Jour.*, 1901, ii, 578.

Male, aged eighteen years. The patient, after eating a pint of cherries, had severe abdominal pain, which at first improved, but after five days became worse. The abdomen became distended, and there was some dulness and resistance in the cecal region. At operation an intussusception was found in the hepatic region. The gut was opened and emptied of a pint of fluid. A Meckel's diverticulum had invaginated into the intestine, and was reduced by finger through an incision. The diverticulum was two feet from the valve. Recovery.

Case 13.—1901. Morison, *Lancet*, 1901, ii, 1047.

Male, aged five years. The patient was seized with acute abdominal pains, coming on in paroxysms and with vomiting. Blood was passed by rectum. There was a sausage-shaped tumor in the left iliac region. At operation an intussusception of the lower ileum was found and reduced. It contained an inverted Meckel's diverticulum, which was removed. The child recovered.

Case 14.—1902. Travers, *Lancet*, 1902, ii, 146.

Male, aged ten years. The patient suffered repeated attacks of abdominal pain in the right side and vomiting. The abdomen was flat, except for a prominence about McBurney's point, where a tumor about 2 x 1 inch in size was palpated. It later disappeared, giving place to an indefinite mass. At operation the ileum was found invaginated three inches into the colon, and was reduced with some difficulty. At its upper end was a lump as large as a filbert, which proved to be an inverted diverticulum, three-quarters of an inch long. Recovery.

Case 15.—1902. Wainwright, *Ann. Surg.*, 1902, xxxv, 32.

Male, aged seventeen years. Illness began six days before admission, with loss of appetite, sense of fulness after eating, and constipation. Worked for five days. On the fifth day he was seized with severe epigastric pain and began to vomit. Enemas returned bloody. On admission to the hospital the abdomen was retracted and board-like, tender over lower part, but no tumor was palpable. Upon incision clear fluid gushed out and an intussusception three inches long was found three feet from the valve, which had at its apex an invaginated Meckel's diverticulum about an inch long. It was removed. Recovery.

Case 16.—1903. Terry, *Lancet*, 1903, i, 961.

Male, aged twelve years. The patient had first abdominal discomfort, soon followed by severe attacks of pain, which was most acute below and to the right of the umbilicus. Stools were loose, watery, and blood-stained. Distention was slight. A sausage-shaped tumor was palpable, running upward toward the liver. It became harder during the attacks of pain, and varied in size from time to time. At operation an invagination, twelve inches long was found, at the apex of which was an inverted Meckel's diverticulum six inches long. Recovery.

Case 17.—1903. Zum Busch, *Centralbl. f. Chirurgie*, 1903, xxx, 733.

Male, aged twenty-one years. Patient had dull pain in umbilical region for fourteen months. The present attack began suddenly, with severe pain, fluid stools, and tenesmus. Later there was almost constant vomiting and blood per anum. The right rectus muscle was tense, and a tumor the size of a child's head was palpable in the ileocecal region. At operation an ileocecal invagination was reduced with much difficulty. There remained a tumor in the ileum, wherefore a meter of intestine was resected, with lateral anastomosis. The tumor proved to be an invaginated Meckel's diverticulum, with a lipoma the size of a hazelnut at its apex. The patient recovered.

Case 18.—1903. Dobson, *Lancet*, 1903, i, 1161.

Male, aged four and a half years. Illness began with acute abdominal pain, vomiting, and discharge of blood and mucus from bowel. In thirty-six hours the vomiting had ceased, the pain became constant, with pulse 120 and temperature normal. There was a soft, tender, movable swelling in the right iliac region, extending upward to the right costal margin. At operation the same evening an ileocecal intussusception was found, with a pedunculated swelling at the apex. Corresponding to this on the surface of the gut was a dimple into which a small mesentery passed. The swelling was an invaginated Meckel's diverticulum. Resection, Mayo Robson bobbin; recovery.

Case 19.—1904. Cawardine, *Lancet*, 1904, i, 505.

Child, aged fourteen months. At operation two days after beginning of symptoms an intussusception was found which had just entered the colon. One invagination was reduced and was found to contain a second invagination, within which was an introverted Meckel's diverticulum. The diverticulum was fifteen inches from the valve. The patient died in collapse.

Case 20.—1904. W. Watson Cheyne, *Ann. Surg.*, 1904, xl, 796.

Male, aged nineteen years. The patient had indefinite abdominal pain for two years. Several of the later attacks were attended with vomiting and diarrhea. The vomitus was greenish or yellow. On admission the abdomen was slightly distended. A week later a distended loop of bowel appeared in the left iliac region, which later appeared as a definite tumor. In the evening the bowels moved and contained no blood. At operation, three days later, an intussusception was found in the pelvis. It was eighteen inches long and was easily reduced. A second invagination presented itself and was easily squeezed out. It proved to be an inverted Meckel's diverticulum. This was resected and a lateral anastomosis done. The gut at the site of the diverticulum contained a longitudinal constriction. The patient recovered.

Case 21.—1907. Coffey, *Ann. Surg.*, 1907, xlv, 42.

Male, aged seven years. There was a history of repeated attacks of cramps beginning at two years, recurring every month, and sometimes more often. The cramps were always accompanied by bloody stools. The present attack began with severe pain and frequent vomiting during the first day. The condition improved, but abdominal tenderness continued. The patient was up a portion of the second day and remained well until the fifth day, when severe symptoms returned. On the sixth day the child entered the hospital. There was no distention. On the right side a mass was palpable, extending under the ribs. At operation reduction proved impossible, and the invagination was resected. There was an inverted Meckel's diverticulum at the apex of the intussusception. The patient recovered.

Case 22.—1907. Jäckh, *Deutsch. Zeitschr. f. Chir.*, 1907, lxxxvii, 192.

Female, aged thirty years. The patient had been ill for six months, with cramping pains almost daily. They had become worse in the last three weeks, and were occasionally accompanied by vomiting. There was moderate distention and visible peristalsis in the middle of the abdomen. There was no dulness nor tenderness. The day following the examination there was a bowel movement. Seven days later tumor was felt at the left of the uterus. At operation an invagination was recognized and was easily reduced, but a nodule as large as an egg remained about one meter above the valve. This portion of the gut was resected. The nodule

proved to be an invaginated diverticulum, which was necrotic at the extremity. The lumen of the diverticulum had become closed, and the gut proximal to the diverticulum was double the thickness of the distal part. The patient recovered.

Case 23.—1907. Bidwell, *Lancet*, 1907, ii, 682.

Male, aged three and a half years. The patient was born with an umbilical hernia, which was repaired at the age of one year. Severe hemorrhage from the bowel four months before present attack. There had been repeated attacks of pain, which came on at intervals of one week. They began in the morning and passed off after two hours. Final attack began as the others, but failed to pass off. Vomiting appeared and a tumor was palpable in the right lumbar and hypochondriac region. At operation an intussusception was found involving the large intestine to the middle of the tranverse colon; it was black and edematous, but was viable and was reduced. Four weeks later it was necessary to repeat the laparotomy. An irreducible invagination of the small intestine was found and resected. The specimen contained an inverted Meckel's diverticulum. Recovery.

Case 24.—1907. von Mandach, *Lancet*, 1907, ii, 1733.

Male, aged two and a half years. No history of previous trouble. The child fell ill with slight dyspeptic symptoms. On the seventh day the bowels became completely obstructed, meteorism developed, and operation was performed. There was a double ileocecal invagination, with an introverted Meckel's diverticulum at the apex. The invagination was reduced, the diverticulum everted, and its lumen closed by purse-string ligatures. Recovery.

Case 25.—1907. Kopyloff, *Mediz. Obosrenje*, Band lxviii, abstracted in *Hildebrandt's Jahresbericht*, 1907, xiii, 765.

An obstruction of the bowel originating from an inverted Meckel's diverticulum. A portion of intestine 60 cm. long was resected. Patient recovered.

Case 26.—1908. Brin, *Bull. et mém. Soc. de chir.*, 1908, xxxiv, 1267.

Female, aged thirty-nine years. The patient had been having attacks two or three times yearly for twelve years. During the past year there had been tenderness between attacks. A pelvic tumor was palpable and was thought to be an inflamed salpinx. Supravaginal hysterectomy was performed. Eight days later she had an attack of acute obstruction. The intussusception was reduced, and an inverted Meckel's diverticulum was evaginated and resected. The patient recovered.

Case 27.—1908. Gray, *Ann. Surg.*, 1908, xlvi, 801.

Male, aged eight years. At five years there was an attack of abdominal pain, with passage of blood by rectum. The present illness began with pain in the region of the umbilicus. There was temporary improvement, but after two days, following a bowel

movement produced by licorice powder, violent pain returned. On the fifth day there was increased pain and absolute constipation, followed the next day by vomiting. No blood was passed by rectum. The abdomen was distended, especially above the navel, which was raised, and at the apex of a dome. There was no rigidity nor tenderness. Under anesthesia a tumor was palpable under the liver. At operation a good deal of straw-colored fluid was found in the abdomen. There was an ileocecal invagination, which was removed from the cecum. The enteric part was irreducible and was resected. The patient died fifteen hours afterward. The resected portion contained an inverted Meckel's diverticulum, at the base of which the intestine was considerably narrowed.

Case 28.—1908. Kothe, *Deutsch. Zeitschr. f. Chir.*, 1908, xcv, 286.

Male, aged twenty-three years. The patient had an attack six months previously. The final attack began suddenly, with pain, vomiting, and chill. Vomiting did not recur. The pain was most severe between the umbilicus and symphysis. There was passage of neither feces nor flatus. When admitted to the hospital on the fourth day the abdomen was not distended, but was slightly tender. The next day tympany became marked, vomiting was violent, and the general condition was much worse. At operation a moderate amount of serosanguinolent fluid escaped from the abdomen. An intussusception was found in the ileocecal region, and as it was irreducible it was resected. The intestinal contents were allowed to flow out of the free end of the gut, and then an end-to-end anastomosis was done. The patient recovered. At the tip of the invaginated diverticulum was an infarcted polyp 6 cm. long.

Case 29.—1908. Kothe, *loc. cit.*

Male, aged seven months. Illness began three days before operation. Vomiting occurred once on the second day. Enemas were used without result; in one the water was returned bloody. There was no tympany, but the abdomen was generally tender, particularly so in the ileocecal region. There was no dulness nor tumor. Under anesthesia a tumor was palpable in the right lower quadrant. At operation a moderate amount of serous exudate escaped. The ileocecal tumor was recognized as an intussusception, which was pushed into the ileum, but the gut ruptured from the manipulation, and was therefore resected. The cut ends were sewed into the abdominal incision. The patient died from exhaustion. There was no peritonitis. Examination of the specimen showed a diverticulum 2 cm. long, which was inverted into the ileum.

Case 30.—1908. Delore et Leriche, *Revue de Chir.*, 1908, xxxviii, 39.

Male, aged six years. Patient had had several attacks of ob-

struction in last year. July 22, 1907, had vomiting of bile, colicky pains, no passage of gas, or feces. Next day pulse was 80, temperature was 38.5°C . and there was a tumor in the right iliac region. July 25, pulse, 115; temperature, 37.8° ; violent colicky pains, bilious vomiting, complete obstruction; no melena. The abdomen was distended and there was a mobile tumor in the left iliac region. At operation (third day after beginning) there was a large quantity of liquid in abdomen. The invagination could not be reduced, was resected, and the intestine joined end-to-end with a Murphy-Villard button. Patient died forty-eight hours later. The piece resected was 40 cm. long, and the intussusceptum was 15 cm. long. The mucosa was gangrenous. There was a depression in the serous surface into which a probe could be thrust 5 or 6 cm.—an inverted Meckel's diverticulum.

Case 31.—1909.—Busch, *Deutsch. med. Woch.*, 1909, xxxv, 1369 and 1370.

Child, aged seven years. The patient came to clinic on the third day of the illness. At operation an invagination was found which reached from 50 to 60 cm. above the ileocecal valve to the hepatic flexure. At the end of the intussusception was an inverted Meckel's diverticulum with a hard nodule as large as a hazel-nut at the apex which proved to be an accessory pancreas. The diverticulum was resected and the patient recovered.

Case 32.—1909.—Riedel, *Deutsch. med. Woch.*, 1909, xxxv, 1655.

Female, aged twenty-five years. The attack began suddenly with severe pain in abdomen and vomiting. There was tenderness at first below the flanks. The diagnosis was perforative peritonitis, with intestinal paralysis. At operation an invagination 20 cm. long was found in the pelvis and was resected. The patient died at the end of the operation from heart failure. The diverticulum was found inverted and partly gangrenous.

Case 33.—1911. Mühsam, *Berl. klin. Woch.*, 1911, xlviii, 1089.

Female, aged five years. The patient had had two attacks of obstruction, which were cured by enemas. The present attack began with vomiting and obstruction. There was a hard, sausage-shaped movable tumor to the right of the navel. There were 30,000 leukocytes. At operation there was an invagination reaching to the hepatic flexure, which was reduced with some difficulty. 20 cm. from the valve was a diverticulum the size of a little finger, invaginated into the bowel. It was everted and resected. The patient recovered.

Case 34.—1912. Drummond, *Ann. Surg.*, 1912, lv, 404.

Male, aged twenty-nine years. Admitted July, 1909 for hemoptysis. He was discharged but soon returned complaining of colicky pains in abdomen, epigastrium, and left hypochondrium. He had occasional griping pains until November, 1910. In December of

same year had renewed abdominal pain with tenderness and distention in the epigastrium. In the following February, after sudden pain in the abdomen with vomiting, a mass appeared in the lower abdomen which increased in size and became harder during the paroxysms of pain. He passed a pint of blood per rectum. Operation February 6, 1910. There was some free fluid in the abdomen and an intussusception four inches from the ileocecal valve. It was easily reduced but a lump remained within, and a portion of intestine was therefore resected, with end-to-end anastomosis. Death February 14, from peritonitis from leak in suture line. Specimen showed a diverticulum three and one-half inches long with a constriction of the gut at the point of its attachment.

Case 35.—*Loc. cit.*

Female, aged three years. The child had an attack every six weeks, for the last nine months, which were relieved by enemas and castor oil. Duration of the present attack, one week. Two hours after breakfast the patient was seized with sudden severe pain about the umbilicus followed by vomiting. No flatus nor feces was passed for two days. On admission pulse was 126; temperature, 99.8°; upper abdomen was distended and peristaltic waves were visible in the region of the umbilicus on right side. There was no rigidity nor tumor. At operation, an intussusception was found and easily reduced except where the diverticulum was inverted into the gut. Diverticulum was reduced and excised. Child died twelve hours later. Diverticulum was one and one-fourth inches long and contained an accessory pancreas.

Case 36.—*Loc. cit.*

Male, aged fifteen years. Four days before admission the patient had an attack of pain in lower abdomen, with nausea and vomiting. Next day bowels moved and he was better. In the evening severe pain and vomiting returned with relief next morning. On the second day following when admitted, he had slight pain and distention, no tumor nor dullness. There was tenderness in left side. At operation an irreducible intussusception of the small bowel was found and resected, with end-to-end anastomosis. Death shortly afterward. At apex of intussusception was a Meckel's diverticulum four and one-half inches long, completely gangrenous.

Case 37.—*Loc. cit.*

Male, aged eleven years. Three days before admission he complained of sudden pain in epigastrium followed by vomiting. No movement of the bowels occurred for two days. Abdomen was distended, tympanitic, and tender. A tumor was palpable by rectal examination. At operation, free fluid was found in abdomen, and an intussusception of small intestine in pelvis. Resection was followed by death. A Meckel's diverticulum one and one-half inches long was found completely inverted and gangrenous.

Case 38.—*Loc. cit.*

Male, aged twenty-five years. The patient had attacks of abdominal pain a few months previously which were relieved when bowels moved. Three days before admission he had a severe attack of pain after drinking water. His bowels moved freely and he vomited. Bowels had not moved since first day of illness. Abdomen was retracted and rigid, with tenderness in the epigastrium. At operation an intussusception appeared which was nearly gangrenous. It was resected, and ileum was joined to cecum by means of a Murphy button. Patient recovered. At the apex of the intussusception was an inverted Meckel's diverticulum four inches long, gangrenous at the tip.

Case 39.—1913. Drummond, *Surg., Gynec., and Obst.*, 1913, p. 656.

Male, aged thirty-four years. In August, 1911, began to have attacks of abdominal pain with rumbling and sometimes diarrhea. In November, attacks became more pronounced. A week before admission the vomit contained blood. For three days before admission he vomited incessantly and complained of pain coming on in spasms. When examined, pulse was 128; temperature, 98°; abdomen was distended, no intestinal movements visible. Rectal examination was negative. Enterotomy was done and death followed in two days from toxemia. Postmortem examination showed an intussusception with a Meckel's diverticulum three inches long at the apex.

Case 40.—*Loc. cit.*

Male, aged eight years. No record of previous attacks is given. The present attack lasted a week, the intussusception was resected and the patient died. A small Meckel's diverticulum, two inches in length was found inverted into the gut.

Case 41.—1913. Turner, *Guy's Hosp. Rep.*, ix, reported by Wellington, *Surg., Gynec. and Obst.*, 1913, xvi, 74.

Male child, aged sixteen months, operated upon by Lane. There was an intussusception in right iliac region, which was reduced and a second found. This was reduced and a third found. The last contained an inverted diverticulum.

The following cases of intestinal intussusception with an invaginated Meckel's diverticulum are recorded, but insufficient details are given.

Treves, *Intestinal Obstruction*. Philadelphia, 1884, p. 215. Specimen in Guy's Hospital Museum, No. 1819 (45).

Treves, *Intestinal Obstruction*, second edition (quoted by Dobson, *Lancet*, 1903, i, 1161). Specimen in Museum of Royal College of Surgeons of England, No. 2718 a.

Adams, *St. Bartholomew's Hospital Reports*, 1891, xxvii, 171. Obscure symptoms of intestinal strangulation had existed about a fortnight. At autopsy an intussusception into the cecum was

found. It contained an inverted diverticulum. Subject was a male.

Willett, *St. Bartholomew's Hospital Reports*, 1891, xxvii, 171. Specimen No. 2183 in the museum of St. Bartholomew's Hospital. Double intussusception of intestine and Meckel's diverticulum in a male.

The following cases are reported as examples of this condition, but are doubtful

O'Conner, *British Med. Jour.*, 1894, ii, 123.

Male, aged thirteen years. Eight days after a severe wetting had two or three rigors, with a temperature of 104°. He was better the next four days, but had no bowel movements, notwithstanding the use of laxative. The next day after the use of opium he passed a portion of the ileum eleven and one-quarter inches long with a Meckel's diverticulum. "The upper portion was invaginated into the lower, the entire length of the diverticulum appearing through the lower orifice."

Boldt, *New York Med. Record*, 1900, lvii, 655. No details given.

Guyot, reported by Forgue et Riche, "Le Diverticule de Meckel," Paris, 1907, p. 89.

Male, aged ten years. Final attack lasted five days. An entero-anastomosis without resection was done. Death. Autopsy showed an ileocecal intussusception with a Meckel's diverticulum.

Brook, *British Med. Jour.*, 1907, ii, 862.

Taeck, referred to by Von Mondach, *Lancet*, 1907, ii, 1733.

Ryan, *Intercolonial Med. Jour.*, Australia, 1907, xii, 459. Male, aged nine years. Onset of illness acute with pain and vomiting. At operation twelve inches of gut near iliac region were resected. The patient died. The intussusception started from a polyp at the apex.

In summarizing the data of these cases one recognizes regrettable paucity of details, especially as to pathology. A comparative study of the physical condition of the gut, as observed at operation in connection with the subsequent history of the various cases, would be of great value in guiding the surgeon toward the best operative procedure.

Points worthy of special notice are age, sex, manner of onset, appearance of tumor, and the relatively slow course.

Age. The age varied from seven months (29) to 39 years (26), the average in the 41 cases quoted being thirteen years. Of these 20, or 49 per cent., were under ten years of age, 10 between ten and twenty years.

Sex. Of those in which the sex is given 31 were males and 7 females, giving a ratio of over 4 males to 1 female.

Previous Attacks. In 17 of the cases a history of previous attacks is given. In none of the other cases is it specifically stated that there were no previous attacks. In those cases in which previous

attacks have been recorded it stands out so plainly that one is disposed to suspect that some of the reporters may have overlooked the importance of a history of previous trouble in the making of a diagnosis. For this reason it seems worth while to examine these histories with some care. The factors worthy of attention are the number of previous attacks, the location of the pain, the presence of a tumor, and the presence of blood passed per anum. In 3 of the recorded cases (5, 27, and 28), a single attack is mentioned, and this was the case in our patient. In 1 (33) two attacks are mentioned. In 9 (6, 14, 23, 26, 30, 34, 35, 38, and 39) many or repeated attacks are mentioned. In 1 case (21) monthly attacks since the age of two years are mentioned, and in 1 (22) the pain is mentioned as having been present continuously for six months. The character of the pain has been described as dull in 1 case (17), colicky or cramps in 6, 21, 22, and in our own case. In 1 case (14) the pain is recorded as having been in the right side, in 2 (16 and 34) about the navel, and in our case just below the navel. In 1 case (14), in which obstruction was diagnosticated a tumor was felt and in our case a tumor was diagnosticated during the existence of the obstruction. Blood was discovered in the stool but twice (21 and 27). It is interesting to note that the ages of these two patients were respectively seven and eight years, a later age than the usual occurrence of simple intussusception.

The Final Attack. The history of the final attack which brought the patient to operation or autopsy (or both) presents much that is interesting. In this, too, as in the history of preceding attacks there is a want of negative history, so that it is impossible to determine if certain cardinal symptoms were absent or whether the historian was ignorant of their interest or importance and failed to make record of their presence.

It is a matter of judgment as to what factors shall be considered of fundamental importance. The nature of the disease indicates what factors are likely to be most prominent and likewise what secondary features are likely to appear. Thus pain may be regarded as the cardinal feature; accompanying this are vomiting and distention as positive results of the obstruction and absence of stool and flatus as negative results. Tenderness and rigidity of the abdominal walls and the presence of free fluid in the abdominal cavity give evidence as to the degree to which the intestine has suffered from its acute malnutrition. Conversely, blood in the stool gives similar evidence of the state of nutrition of the mucous membrane. With this general scheme in mind we may proceed to investigate our evidence.

Pain. We may assume that pain is present in every case and our interest lies in its character and location. It is usually colicky in character, and is located usually about or below the umbilicus

or in the right side. The pain bears evidence of the preponderance of traction in the production of symptoms in the condition in question as compared to some other type of obstruction. It is intense, cramp-like, and is disposed to intermission. Usually there are periods of nearly or quite complete freedom from pain. It is not attended by evidence of inflammation and collapse.

Vomiting. In 24 cases this symptom was reported present. In 1 case (18) it is stated to have been present the first thirty-six hours, and in 1 (21) for the first day and in 1 (32) at the beginning. In 1 (27) it is not noted until the eighth day. The character of the vomitus is usually dark green or yellowish. In 1 case (39), the vomit a week before admission contained altered blood. Vomiting, compared to many types of intestinal obstruction, is characterized by its moderate intensity.

Meteorism. The relation of this symptom of vomiting is indicated by the fact that in all but 5 of the 23 cases in which there was vomiting, meteorism likewise is recorded. In 2 of the 3 exceptions meteorism is stated to have been absent, and in the others it is not mentioned. The records on this point are rather striking, inasmuch as in this disease meteorism never appears to be pronounced. Possibly this is because at the time of obstruction distention of the gut seldom reaches a degree comparable to instances in which paralysis is a factor.

Tenderness. This symptom is usually associated with the previously mentioned phenomena of vomiting and distention. It is less often present, however, for in 3 cases it is stated to have been absent, while both tenderness and meteorism were present. In our case tenderness was present but not marked. It is nearly always a late symptom.

Rigidity. In 1 case (15) only is rigidity stated as being board-like, and in 1 (17) the right rectus was stated to have been rigid. In Case 38 the abdomen was rigid and retracted. In our case the right rectus was more rigid than the left, but yet lacked the rigidity of a response to an inflammatory process. On the whole it is a negative sign.

Abdominal Exudation. The presence of a free exudate was noted in 10 and 32 and was well marked in our case. In a number of other cases it is stated that a quantity of fluid escaped when the abdomen was opened, though no note was made of it previously. In these it is more than likely careful examination would have shown free fluid in the flanks. Its value as a sign consists in that if its presence is detected it may mislead the observer to believe that an inflammatory exudate is present.

Blood in the Stool. In 12 it is specifically stated that blood was present in the stool, but in each instance the amount was but slight, except in Case 34 in which a pint of bright blood was passed. In 4 (2, 23, 27, 30,) it is also specifically stated that there was no

blood. The same is true in our case. When blood is present tenesmus is not marked.

Tumor. The most typical factor in the picture of the disease is the presence of tumor. Tumor is stated to have been present in 20 of the recorded cases. In our case the attending physician was able to palpate tumor on the third day, but when the patient came into our hands none could be felt because of the distention. Dulness and resistance were noted in the right flanks of two additional cases (2 and 12). In 2 cases it is specifically stated that no tumor could be felt (2 and 15). In 2 cases (10 and 29) tumor was felt under narcosis. The location of the tumor is interesting. The most frequent location is in the ileocecal region, where 7 were found and next in frequency were 2 in the hepatic region, while 4 were in both these regions, beginning in the ileocecal region and extending to the hepatic region. In 2 cases (3 and 34) the tumor was located below the navel, once (7) in Douglas' pouch, once (22) to the left of the uterus, once (37) felt per rectum, and in our case to the right of the umbilicus. The tumor is sometimes described as sausage-shaped, sometimes movable, and sometimes variable in size and consistency.

Duration of the Disease. The time the disease had existed from the beginning of the illness until it came under observation varied from twenty-four hours (8) to twenty-eight days (10). One was thirty-six hours (6), 2 were forty-eight hours (19 and 34), 7 (13, 28, 29, 30, 31, 37, 38) were three days, 1 (36) was four days, 1 (3) was five days, 2 (15 and 21) six days, 5 (24, 27, 35, 39, 40) seven days, 1 (23) eight days, and our case was five days. This bears evidence that the malady is but moderately acute and accounts for the modified form in which some of the cardinal symptoms of obstruction appear—notably, vomiting and meteorism.

Diagnosis. From the foregoing it is evident that the material out of which to construct a diagnosis has varied in the different cases. It is worth while to summarize this material and to compare it with groups of analogous symptoms produced by other diseases. Pain is the prominent symptom, is usually the earliest to appear, and is the most persistent. The characteristic feature is its cramp-like intermittent character. Its location is usually in the middle of the abdomen, sometimes more to the right side. To pain the evidence of obstruction is soon added, usually vomiting first. This may be early, when it is a reflex from the cramp-like pain or later, when it is the result of the accumulating intestinal contents. In the former case the vomitus may consist of food or greenish mucus, and in the latter of large quantities of yellowish or brownish fluid. With these indications of abdominal storm the lack of abdominal tenderness and muscle rigidity, coupled with a normal or subnormal temperature, marks the condition as some disturbance of the fecal current. The presence of repeated disturbances

leading up to the attack with the above symptoms should give some hint as to the nature of the malady. Our own case had all the ear-marks of the disease and should have been diagnosticated if we had but had the opportunity to study the recorded literature before proceeding to operation.

Differential Diagnosis. This disease may be mistaken for obstruction due to other mechanical causes or to abdominal disasters, mostly inflammatory, which interfere with the dynamics of the intestinal tract in an indirect way.

The causes for obstruction which might come into question are the various internal hernias and strangulations, notably those dependent upon a looping of the gut about a band. These bands may be inflammatory in origin or may be due to congenital anomalies, such as a Meckel's diverticulum attached at both ends. Some of the internal fossæ may ensnare a loop and give rise to similar symptoms. Furthermore, these conditions may give a history of repeated attacks almost like those of intussusception. The presence of a tumor, however, will exclude the probability of band obstruction and to a less degree that of fossa obstruction. Intussusception without diverticulum usually occurs in the first year and a half of life, so that in these cases one can assume the presence of a Meckel's diverticulum only when there is a hard nodule at the head of the intussusception or some deformity at the umbilicus. It is presumed that any surgeon sufficiently advanced in his profession to have any acquaintance with the literature of intestinal obstruction would not fail to exclude hernia of the external openings.

The inflammatory lesions of the abdomen usually present symptoms plainly divergent from those of the affection under discussion, yet because of their frequency they are likely always to be present in the surgeon's mind. Perforative lesions are regularly attended by sudden pain, but it is not cramp-like and remissions are not apt to intervene. The practitioner, to be sure, may cause perforation to simulate intussusception by giving morphin, and may thus confuse the surgeon. Tenderness and rigidity also in this way may be suppressed, but it is not usual for an abdomen which is the site of an inflammation severe enough to demand large doses of morphin to quiet down under its influence sufficiently to obliterate all evidence of tenderness and resistance. The general appearance of the patient may give evidence of a severe inflammatory lesion in the belly, and even if the distinctive symptoms are neutralized by morphin, an expert clinician should be able to read the patient's true condition in his face. As in all cases of obstruction the absence of reactive manifestations is a most important differential point. The absence of accelerated pulse rate and the normal or subnormal temperature are very suggestive. In this respect, however, fallacies beset the diagnosis from two directions. Other abdominal lesions such as perforative appendicitis may show little

or no reaction, and in the late stage of the disease under discussion the pulse may be rapid and the temperature may rise.

The diagnosis in complicated cases is thus not to be made upon general evidence, but upon the consideration of the special features of individual cases. If the disease has been determined to be surgical it is important to decide between an obstruction and an inflammatory lesion, for upon this decision depends the position of the incision. That this is not always easy is shown by the late hour at which so many cases reach a final solution, often indeed at autopsy. Lesions not surgical in character, which are capable of giving a like series of symptoms, are numerous. The early age of most of these patients excludes the two diseases, aside from frank inflammatory conditions, which most resemble obstruction—namely, gall-stones and pancreatic disease. The ephemeral nature of the acute intestinal colics should differentiate them at an earlier date than has been done in most of the reported cases. The fact that some of the cases of the disease under discussion had been preceded by a series of slighter attacks naturally leads to delay in the hope of the same favorable outcome. That blood in the stool should be ascribed to dysenteric diseases is excusable, since in this affection the pains are often diffuse over the abdomen. In dysentery the passage of mucus and stool is accompanied by tenesmus, but in intussusception blood passes without tenesmus unless the inverted gut approaches the anus in which event it may be reached by the palpating finger. After tumors appear or meteorism gradually ensues delay should not be countenanced.

Pathogenesis. The factors responsible for the invagination of Meckel's diverticulum have been the subject of much speculation. The one essential is that the distal extremity of the diverticulum be unattached. It has long been known that the floating diverticulum is subject to a variety of accidents, of which torsion has been the most common. The blood supply being derived from the small intestine usually opposite its own source of supply makes the nutrition of the diverticulum at all times somewhat precarious. That gangrene about the base should occur need therefore occasion no surprise.¹ To what degree such accidents may be responsible for the various narrowings and thickenings at the attachment of the diverticulum and of the intestine itself is open to question. Gray (24) believes that such accidents are responsible for their existence. Careful histologic study which might throw some light on the subject is lacking. That some of these anomalies are congenital is quite likely. Even though it is granted that they are the result of pathologic processes, the mechanics of inversion is not explained. Küttner² was of the opinion that in his case of inversion of the diverticulum an accessory pancreas at the tip of

¹ Gray, British Med. Jour., 1907, ii, 825.

² Beitr. z. klin. Chir., 1898, xxi, 289.

the diverticulum was responsible. He thinks that a polypus or a fecal mass might act in the same way. Accessory pancreases were present in Brunner's (8) case and in one of Drummond's (35), and a small lipoma was present in Zum Busch's. In Moroni's case (5) the diverticulum contained a fibrous polyp. Gray believes the presence of such a tumor would prevent rather than assist in the production of inversion. De Quervain (2) believed the rush of fluid along the intestine produced a negative pressure sufficient to produce an invagination. Gray (27) believes invagination begins at the base of the diverticulum, congestion at this point as the result of torsion causing swelling and mucus production being, according to him, the fundamental factor. That the mucosa is loosely attached is proved by Hohlbeck's (10) case in which the mucosa alone was invaginated. A narrowed base would permit an accumulation of contents, which when forced by active peristalsis into the lumen of the gut, might easily be accompanied by mucosa and this would ultimately drag the musculature after it. Intussusception might then follow immediately or sometime later.

The study of our case and of the literature would lead us to believe that intussusception of the gut at the point of attachment of the diverticulum is the first event and that inversion of the diverticulum occurs as a secondary process. A thickening of the gut wall at the site of attachment of the diverticulum might readily give the stimulus to such a course of events. That such an event is mechanically possible is illustrated by a case recently reported by Kasemeyer,³ in which a carcinoma of the cecum became the apex of an intussusception. Other like instances have been reported. When a foreign body is to be propelled along the intestine this is accomplished by a relaxation of the wall in front of the object and a contraction behind it. If the thickening in the intestinal wall project within the lumen the physical characteristics of a foreign body within the intestine are produced. Such a thickening may occur within the diverticulum leading to a primary inversion of the diverticulum or it may occur about the base of the diverticulum in the wall of the intestine proper leading to an intussusception without an inversion of the diverticulum. It is only by such a mechanism that an inversion without intussusception or an intussusception without inversion can be explained. There must be a course common to them both. That such changes do occur is demonstrated by our case. Partial inversions or beginning intussusception would explain the repeated slighter attacks.

Treatment. Obviously treatment must be surgical. Enemas can hardly find a justification at the present time. The ideal procedure is reduction of the intussusception and eversion of the invaginated diverticulum, to be followed by the resection of the

³ Deutsch. Zeitschr. f. Chir., 1912, cxviii, 205.

diverticulum. In order that this may be carried out the gut in all its portions must retain its integrity so as to permit the necessary manipulation, and the circulation must be in such a state as to maintain the nutrition of the gut after the treatment is completed. The invagination may be irreducible or the gut when relieved of its intussusception may not be viable. These possibilities must be judged at the time of the operation, for the state of the gut is dependent upon the duration and the degree of constriction to which it has been subjected. The former factor only is known in a given case. The treatment is divisible, therefore, under the following heads. (1) "When the gut is reducible and viable," and (2) "when irreducible or reducible and not viable."

When Reduction is Possible. In these instances the reduction of the intussuscepted gut is attempted by gentle pressure from above with the guarded assistance of traction from below. In some instances it has been easily accomplished, as in Cases 7, 8, 9, 10, 17, 19, 20, 22, 24, 26, 29, 31, 34, 35, and 41; while in Case 14 some difficulty was experienced. This may be said of our case. In Case 33 reduction was accomplished with difficulty. The diverticulum was reduced in Cases 19, 20, 24, 26, 38, and our own case. In none in which the intussusception was easily reduced was resection necessary except in Case 17, which was reduced easily and then resected, and in Case 29, in which the bowel was torn by the manipulation. It would seem therefore that if the gut is easily reducible it will be in such a condition that resection will not be required. In 1 case, however, (33) reduction was possible, yet gangrene occurred, requiring a secondary resection.

When the gut is reducible the problem of viability must be decided. The problem here is no different from that in any other case of intestinal obstruction. If the gut is in active peristalsis, after being released, it is viable. Slight peristalsis, according to Gaardlund⁴ may occur in a gut which subsequently becomes gangrenous. Mesenteric thrombosis and great edema of the gut wall indicate impending gangrene. A deep lusterless black indicates necrosis. Less degrees of discoloration are compatible with restitution and one or more of the usual means for determining the point may be employed. These are chiefly the temporary use of warm compresses, the temporary exclusion of the suspicious loop without the abdominal cavity, and provision for drainage about the replaced loop, with the hope that should integrity fail external drainage will rescue the patient.

Gaardlund,⁵ in a very carefully studied case, has called attention to the fact that the mucosa may be injured beyond repair when the musculature is still apparently viable. This is capable of producing delayed disaster. Reports of fatal cases are not full

⁴ Arch. f. klin. Chir., 1912, xcviii, 433.

⁵ Loc. cit.

enough to permit a judgment as to whether or not a too conservative procedure has been responsible for deaths. Information as to the state of the mucosa in fatal cases in all types of obstruction is much desired.

When the Gut is Irreducible. Resection obviously must be practised if reduction is not possible or if injury is inflicted upon the gut in the process of reduction. Thus in Cases 1, 2, 3, 4, 6, 11, 13, 15, 17, 18, 21, 23, 25, 29, 30, 32, 36, 37, 38, and 40 resection was done. When the gut is irreducible or if reducible, obviously unviable from gangrene or thrombosis already present or inevitable from injury to the mesentery or the gut wall inflicted during the effort at manipulation, a solution of continuity of the intestinal circulation is unavoidable. Three plans are open to the operator. (1) An artificial anus may be made proximal to the point of obstruction, allowing for the removal of the irreducible mass and the reestablishment of the intestinal canal at a future date, or (2) the mass may be resected and the free ends of the gut brought externally, either with or without the employment of Paul's tubes, leaving the establishment of the gut continuity to a subsequent date, or (3) the mass may be resected at once and an anastomosis made.

In solving problems of treatment one must be guided by the experience of one's self and of others in the same class of cases and in allied cases which present analogous features. The personal equation of the operator here will have free play.

Reasoning from analogy it would seem that if the novice should meet such a problem an artificial opening would afford the patient the best chance of life. The same is true in the hands of the more expert when working under exceptionally unfavorable conditions. In other conditions resection of the offending mass should be done. Immediate anastomosis may or may not be done depending on the condition of the patient's intestinal tract. If the patient is still possessed of good power of peristalsis a skilful operator may proceed at once to anastomosis. If the gut has little or no visible power of propelling its contents, anastomosis would better be deferred. Unquestionably the stagnating intestinal contents will flow out of a Paul's tube with greater facility than through a new anastomosis opening and will be much sooner beyond the reach of avenues of absorption. Greater moral courage is required to quit than to go on.

If we try to substantiate these views from the recorded histories we are met by the fact that operators, except in a few cases, have chosen to do an immediate anastomosis, a fact which one could divine from reading the outcome of these cases.

Of the resected cases in which definite information is available 13 died and 9 recovered, which represents a high mortality; 5 of these cases came to operation in six to eight days, indicating a subacute process and one on the second (17), 5 on the third (13,

28, 30, 37, and 38) day and one (36) on the fourth day. One in which drainage was done (12) recovered and 1 (39) died. Of those in which reduction was possible, necessitating the removal of the diverticulum only, 9 recovered and 4 died. The better operative prognosis in the cases in which injury to the gut is slight is obvious.

The cause of death in those where reduction was possible and resection was not done remains to be determined. In Gaardlund's case reduction was possible, but secondary gangrene took place and he saved the patient by a secondary operation.

For the reduction of the mortality one must apparently look in the direction of a closer study of the advisability of resection when the gut is reducible or the question of drainage and temporary resection where the gut is certainly lost. More radical procedure in some of the simpler cases and more conservative procedure in the very grave cases seem to be the lines along which we may hope to advance to a better prognosis.

SPINAL GLIOSIS OCCURRING IN THREE MEMBERS OF THE SAME FAMILY, SUGGESTING A FAMILIAL TYPE.¹

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THE following cases present not only an unusual symptom group, but are chiefly of interest owing to the development of the condition in three members of one family, two brothers and a sister. One of the cases, C. S., a boy, aged thirteen years, came under my observation in May, 1912, following his admission to the neurological service at the Jefferson Hospital. The other cases, P. S., female, aged twenty-four years and E. S., male, aged twenty-two years, were studied in November of the same year. As the symptoms were practically identical in all three patients, one, the eldest, will be recorded in detail as illustrating the condition:

P. S., female, aged twenty-four years, single. She had the usual diseases of infancy and childhood and an attack of influenza when sixteen. Her menses began at the age of sixteen years and were regular and not especially painful. When she was aged about eight years a small sore appeared on the second toe of her right foot; her mother, thinking the sore contained a splinter, opened it and removed a small spicule of bone, the wound subsequently healing rapidly. Two years later a similar condition developed on the

¹ The cases were presented before the Philadelphia Neurological Society, November 22, 1912.

second finger of the right hand. The patient states that she does not remember ever having been able to button her clothing at the back, nor has she been able properly to recognize touch, pain, heat, or cold on her hands and feet, but can recognize these sensations readily on other parts of her body. That all forms of sensation were lost in the affected areas was elucidated in the physical examination.

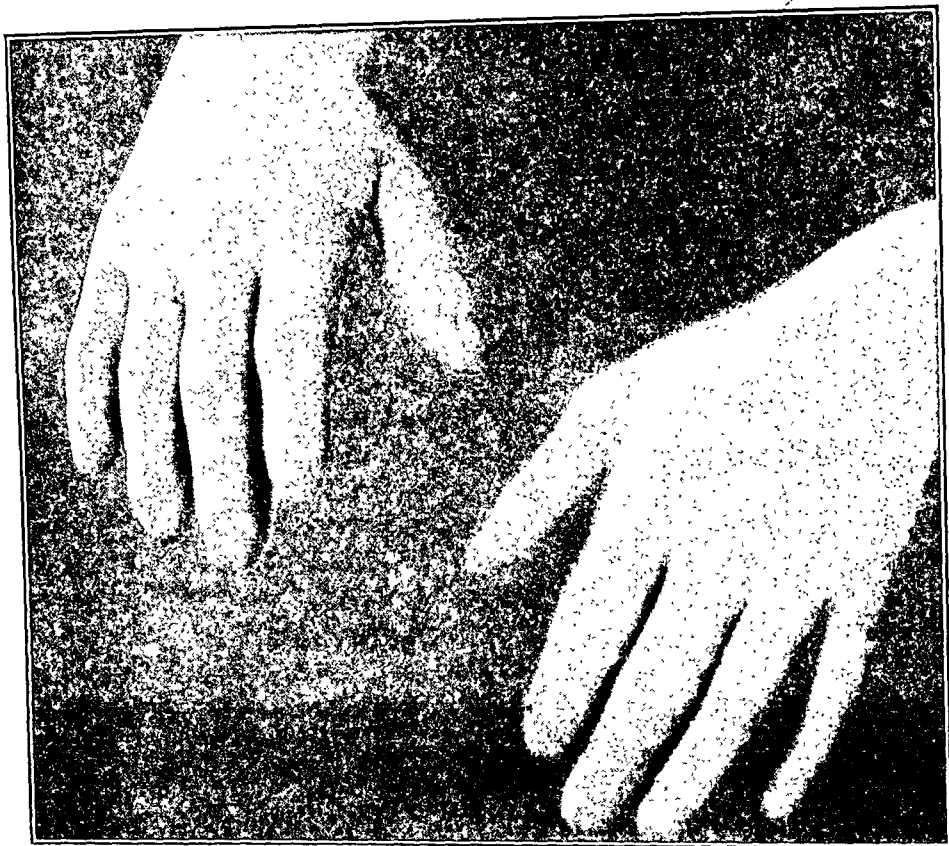


FIG. 1.—Hands of C. S., showing clubbing of fingers and trophic changes of nails.

EXAMINATION.—The fingers of both hands show marked trophic changes, some being affected to a greater degree than others. The fingers most involved show spontaneous amputation of the distal phalanges, either partial or total. The ends of the fingers are clubbed, and where the nail remains it is thickened, and presents marked transverse ridges. The skin over the hands is markedly thickened. All of the joints of the fingers are enlarged and stiff, the second joint of the middle finger, right hand, showing the most distinct arthropathy. The right foot is clubbed; the great toe is absent and the second toe partially gone; the other toes are deformed and displaced upward and backward. The foot is red-dened and macerated, showing an inflammatory condition, due to a secondary infection, with some swelling and edema of the ankle and leg.

The left foot shows loss of the little toe and partial loss of the other toes; a scar on the inner side of the base of the great toe indicates the site of extrusion of a spicule of bone. The joints of the toes of both feet present changes similar to those described as occurring in the finger joints.

All forms of sensation are entirely lost over both hands; from wrists to elbows, sensation is preserved but diminished; from elbows to shoulders, sensation is slightly diminished. In the lower extremities all forms of sensation are lost over the feet, ankles, and lower third of both legs; from this point to just above the knees sensation is preserved, although diminished, and then is but slightly diminished to the hips. Over face, neck, and trunk sensation is normal.

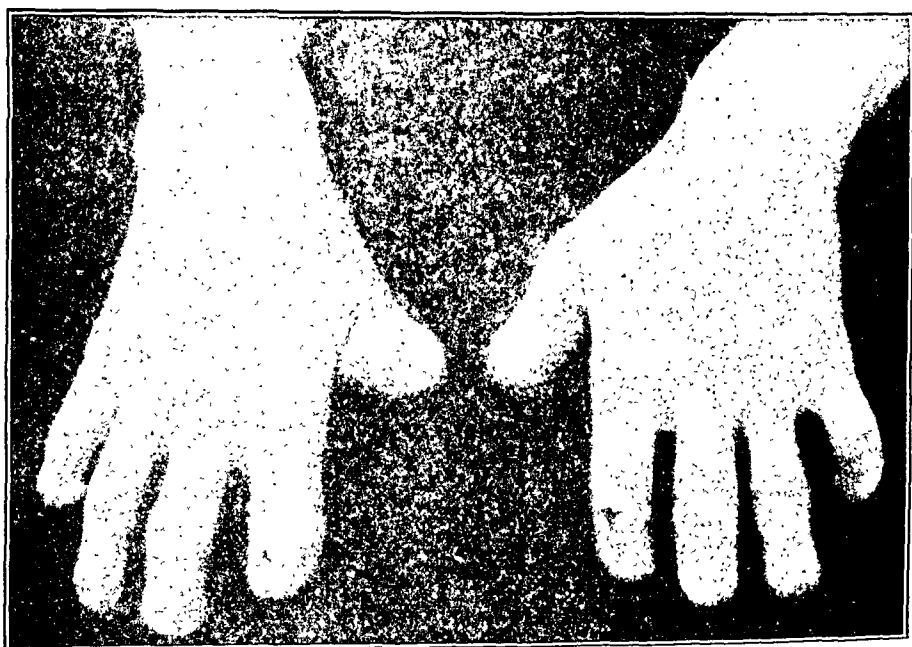


FIG. 2.—Hands of E. S., showing loss of terminal phalanges and enlargement of joints.

The gait is halting, owing to the inflamed and deformed foot, but is otherwise normal as is also the station. There is no muscular wasting, and the patient presents no tremors, palsies, contractures, nor spasticity. There is no scoliosis. The reflexes of the upper and lower extremities are all absent. Babinski's sign is absent; neither is there ankle clonus. The nerves and bloodvessels of the extremities present no gross abnormalities. Mentality is normal.

One of the cases, C. S., presented in addition to the changes described above, superficial ulcers, varying in size from a quarter to a half dollar, over both lower extremities from ankles to knees, chiefly over the anterior border of the tibiæ, also a couple of smaller ulcers over the insteps. These were trophic in character, and the result of trivial contusions, as the boy was very active physically.

Eye examinations were made by Drs. Le Fever and Shannon, and proved to be negative except in the case of E. S., who had concomitant squint (functional) of the right eye.

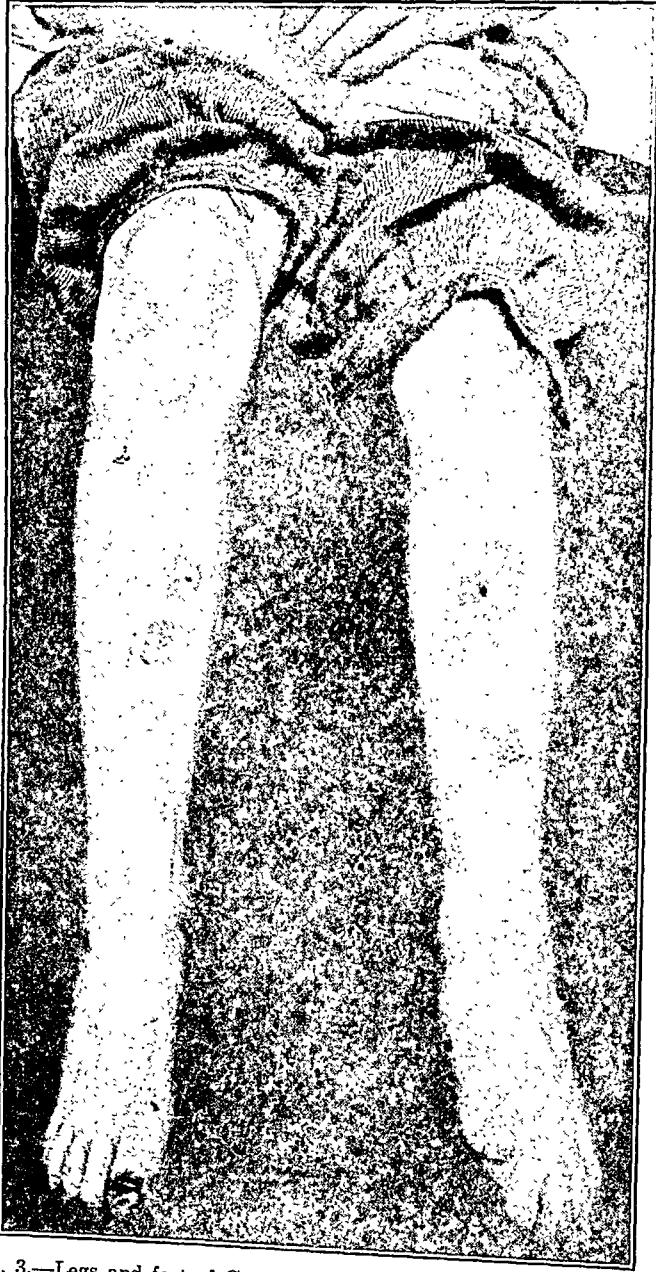


FIG. 3.—Legs and feet of C. S., showing superficial trophic ulcers, etc.

Urinalyses were negative in all three cases, and the blood findings were normal except for a slight diminution in the number of erythrocytes and relative decrease in the amount of hemoglobin, which were not sufficient to be of any pathological significance. A Wassermann test in each case was negative.

An x-ray examination of the right foot of P. S. and the right hand of E. S. was made by Dr. Manges, which revealed trophic changes in all of the bones of the foot except the os calcis, astragalus, and scaphoid. The terminal phalanges of the hand were similarly affected.

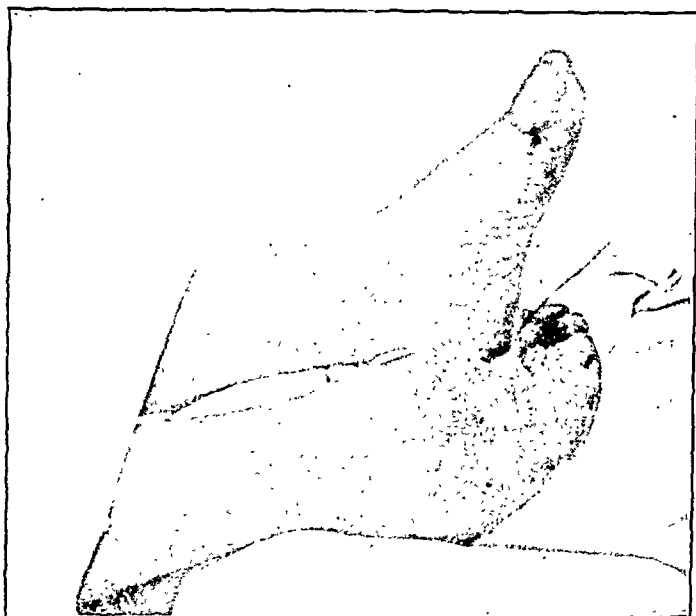


FIG. 4.—Feet of P. S., showing ulceration, loss of terminal phalanges, secondary infection, etc.

Investigation of the family history failed to disclose any possible etiological factor. The father and mother were living and well, having beside the three affected children, two other children, aged five and six years respectively, in perfect health. There was no history of nervous or mental disease, alcoholism, tuberculosis, or consanguinity in the family. It should be noted that the two healthy children have not reached the age at which the symptoms first appeared in their sister and brothers.

The system-complex presented by the above cases is comparable to the condition described by Morvan in 1833 as occurring among the fishermen in Brittany. Joffroy and Achard, Thomas, and others have since demonstrated central-cord cavities in this affection and a peripheral neuritis has also been observed by Joffroy and Achard and by Gombault. These findings have led to Morvan's disease being considered as a form of spinal gliosis associated with peripheral neuritis. Bernhardt and Jolly many years ago called attention to the absence of any fundamental difference between Morvan's disease and syringomyelia. Gowers in discussing the

nerve changes in this affection says that we must consider whether these changes are of developmental origin, and adds, "It is quite possible that they may share the condition of arrested development, entailing a liability to later morbid changes."

In considering the diagnosis, Raynaud's disease was excluded by the absence of the characteristic vasomotor changes and the presence of whitlows with the loss of sensibility. In sclerodactyla there would be no loss of sensation nor spontaneous amputation of fingers and toes.

Anesthetic leprosy was also considered, but cutaneous pigmentation was absent and the sensory disturbance was segmental instead of corresponding to peripheral-nerve distribution. In confirmation of this, Drs. Stelwagon and Gaskill, of the dermatological department of the Jefferson College, examined the cases and reported that the lesions were not those of leprosy.

The writer has been unable to find any instance of the syndrome occurring in two or more members of one family, and considers that the marked familial tendency exhibited in the above cases suggests the possibility of a new familial type.

THE TECHNIQUE OF ABDERHALDEN'S PREGNANCY REACTION.¹

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ABDERHALDEN,² through his studies into the manner in which the animal body protects itself against alien material which gains access into the blood stream, has evolved the theory that the blood plasma, when the tissues are stimulated by the invasion of such foreign substances, acquires enzymatic properties which do not normally exist; that the enzymes so produced act as protective agents by splitting the complex and harmful antigenic carbohydrate, fat, or protein molecule to assimilable cleavage products of the same, as occurs normally in the gastro-intestinal tract; that these enzymes are specific in character for their particular antigenic molecule; that the action of such ferments may be studied extracorporeally; and finally, that their presence may be demonstrated by physical and chemical means.

He has recently applied³ these discoveries in the demonstration

¹ The observations upon which this contribution is based were completed April 1, 1913.

² Schutzfermente des tierschen Organismus, J. Springer, Berlin, 1912.

³ Münch. med. Woch., lix, No. 24; *ibid.*, lix, No. 36; Deutsch. med. Woch., xxxviii, No. 46.

of the specific proteolytic enzyme induced by placental tissue as a means of diagnosing pregnancy. The extracorporeal demonstration of such a specific enzyme is effected by bringing together some blood serum of the suspected subject and prepared placental tissue derived from the same or a closely allied species. If the enzyme is present, cleavage of the placental protein content takes place under favorable conditions; if absent, no such cleavage occurs under analogous circumstances. If the enzyme is present, the subject is considered pregnant; if absent, non-pregnant. The presence or absence of cleavage of the placental protein content is detected in either one of two ways: (1) By accurate polariscopic readings of the suspected serum in the presence of prepared placental tissue, both before and after a period of incubation of these two substances. The readings are identical in the absence of cleavage, whereas a change in the degree of rotation indicates splitting of the protein molecule. This method requires a very accurate and expensive polariscope. (2) The second method for the detection of cleavage employs a semipermeable dialyzer whose pores are sufficiently large to admit of diffusion on the part of the cleavage products of the placental protein, but impermeable to the intact placental protein molecule. Prepared placental tissue and a portion of the suspected serum are placed in a dialyzer. After a period of incubation the cleavage products are tested for in the dialysate by means of the biuret reaction or a modification of the same.⁴ If the characteristic color reaction is obtained, cleavage and dialysis of the cleavage products have taken place, while no visible chemical reaction indicates the absence of cleavage.

Though my cases so far are too few (thirty to thirty-five, including control cases) from which to draw any definite conclusions, there are certain details in the technique upon which little if any stress has been laid which have manifested themselves as being most essential to obtaining reliable results. Moreover, there are some features which, even more than the original procedure,⁵ place the method in the hands of those without a well-equipped laboratory. For these reasons it has been thought advisable to bring them to the attention of others at this stage of the investigation, rather than delaying until the conclusion of the series.

Foremost among the tendencies to vitiate results are putrefactive changes, which artificially split the placental protein to dialyzable decomposition products yielding a positive biuret reaction. A few drops of toluol, as suggested by Abderhalden, added to the dialyzer and to its container at the beginning of incubation have been found insufficient to invariably prevent

⁴ Abderhalden advocates the use of tri-keto-hydrindenhydrate (marketed by Farbwerke-Hoechst Co. as "Ninhydrin," from the Japanese, meaning pregnancy). This reagent has been the one of choice in this series.

⁵ For this procedure the reader is referred to Abderhalden's own articles, already cited.

putrefaction, particularly at 37° C., when that amount of preservative soon evaporates, leaving the tissue, serum, dialyzer, and dialysate unprotected from invading microorganisms. A generous layer of toluol to both the contents of the dialyzer and its container has gone far to correct this error.

Again, the method of storing the dialyzers as suggested by Abderhalden proved but a means of allowing them to become a nidus for putrefactive bacteria when any attempt was made to use them for more than a single test. If, however, after each experiment the following method is employed, dialyzers may be repeatedly, though not indefinitely, used for subsequent examinations. Thoroughly cleanse dialyzer and container after each test in tap water, allowing both to soak in the same for a few hours, to remove all traces of protein from the surface and pores of the dialyzer. Place the dialyzer in the container and submerge the former in distilled water. Plug the mouth of the container with cotton and sterilize the whole in an autoclave or steam sterilizer, after which the entire apparatus may be conveniently stored, awaiting future use, when, except for pouring off the excess of distilled water, it is ready for another experiment. It has been found that this has been a considerable saving of both time and material, while putrefactive errors have been greatly reduced.

A third precaution against putrefactive error early suggested itself, that is, the possible putrefaction of the stock of placental tissue. It may be overcome by the use of either of two controls for each set of tests made. The supernatant water of the stock placental preparation may be tested for the biuret reaction each day tests are to be made. If suggestively or definitely positive, treat the tissue as though freshly ground placenta, boiling with changes of water until the biuret reaction has entirely disappeared. If putrefactive changes are marked, the entire preparation should be discarded. The same error can also be detected by incubating a portion of the tissue in the presence of sterile saline solution instead of serum in a control dialyzer, testing the dialysate at the end of incubation for the biuret reaction. Either of these simple controls not only prevents a possible error in the result of the test, but also materially increases the longevity of one's placental preparation. One at hand is perfectly serviceable after four months have elapsed since it was first prepared.

Finally, on the ground of putrefactive vices the serum for the tests should be collected and handled throughout with at least an approximately aseptic technique.

An error of different origin, of which no mention in the literature has been observed, at least specifically, is that relative to the variations encountered in the permeability of the dialyzers. Schleicher and Schüll's Diffusions-Hülsen, No. 579, the ones recommended as most applicable for the purpose in hand, are in my experience

not proof against disastrous errors, unless certain precautions are exercised. In the first instance, not all such dialyzers are impermeable to normal serum, which, passing through into the dialysate, imparts to it a biuret reaction. To eliminate this error each dialyzer should be subjected to a preliminary "try out," with either blood serum or a serous effusion. All those permeable to such material should be summarily discarded. The period of incubation for this "try out" should obviously be the maximum—sixteen to twenty-four hours at 37° C.

The reverse of this fallacy, the non-permeability of the dialyzers to proteoses and peptones which roughly correspond to the cleavage products of the complex placental protein, is not only conceivable but has been encountered in many of the second "try outs," with an aqueous solution of Witte's peptone, which has invariably preceded the use of all dialyzers employed in this test. The period of incubation for this determination should not exceed the minimum time—twelve hours.

A further control of the permeability of the dialyzers is recognized in the literature. This consists of testing a portion of each individual serum used in a pregnancy experiment to determine if the selected dialyzers are permeable to that particular serum. It is noteworthy that since the adoption of the preliminary "try outs" already outlined, but one serum has been encountered which has permeated the selected dialyzers. On the other hand, before the preliminary "try outs," when all dialyzers were accepted as suitable, so bizarre a result as a positive test and negative control accompanying it occurred in an experiment with my own serum.

Due to a gradual increase in the permeability of the dialyzers, occasioned doubtless by their repeated subjection to heat, it has been found advisable to ascertain their continued impermeability to serum, after about every tenth sterilization, or the dialyzers may be discarded irrespective of their possible future value after the tenth sterilization.

The real danger of an erroneous diagnosis through the failure of observing these precautions makes of them essential controls in the performance of the reaction.

The inherent faults encountered in the dialyzers recommended led to a trial with home-made celloidin ones. About 6 c.c. of oil-free celloidin were poured into glass cylinders about 10 cm. high and 3 cm. in diameter. The entire inner surface of the cylinders was coated with this as evenly as possible, by rotating and inverting the cylinders, so long as the celloidin remained plastic. When no longer plastic, the celloidin was allowed to set quite firmly, thus forming a hollow cast of the glass cylinder. The upper margin of the cast was then cut around its entire circumference about 2 cm. below the rim of the mould. The lateral walls of the sack were then gently freed from the investing cylinder and gently

removed from it. The separation of the mould from the cast as the process advances is facilitated by keeping the dead space between them filled with water.

Though none of the dialyzers so obtained were impermeable to proteoses and peptones, about the same proportion were permeable to serum albumin as the parchment ones. They have the marked disadvantage of standing sterilization by heat very poorly and appear to be reliable for but the necessary "try outs" and one or, at most, two tests. The apparatus, however, does serve perfectly well when the recommended dialyzers are not available.

The dialyzers submerged in water and placed in their container as before may be adequately sterilized by boiling them for twenty minutes in a covered stew-pan instead of using an autoclave or steam sterilizer.

Any good water free from organic matter may safely be substituted for distilled water.

The necessity of incubating specimens at a constant temperature of 37° C. or thereabout for from sixteen to twenty-four hours would require a thermostat for the performance of this test, but it was found that the temperature of a warm room gave about as pronounced a reaction as controls kept in the thermostat, provided that the incubation time of the former was increased to about thirty hours.

As containers for the dialyzers urinometer cylinders or those used in the making of the celloidin sacks serve capitally.

A few controls with a 0.25 per cent. copper sulphate solution demonstrated that all but the slightest degree of dialysis is detected by the biuret reaction as well as by the employment of "Ninhydrin." A greater accuracy in observation is, however, required for the former.

The collection of blood should be by venipuncture. Though the use of a MacRea or Keidel tube is very convenient, a hypodermic syringe of sufficient capacity (6 to 8 c.c.) or even a large hypodermic needle and a sterile test-tube answers all necessary requirements, asepsis and the procuring of hemoglobin-free serum.

Though the foregoing simplifications are not ones of choice, they bring the test within the reach of those not engaged in laboratory practice on a large scale.

My first applications of this serum test for pregnancy were most disheartening, the laboratory findings and the clinical diagnosis being at variance most of the time. The adoption of the foregoing precautions has, however, yielded equally gratifying results. The cases examined, though not many, have covered a considerable range of ground, being positive as early as the seventh week of gestation and constantly so from then on to well into the puerperium. The time of the disappearance of the reaction after delivery has been between the seventh and twentieth day of the

puerperium in those cases in which this point has been investigated. Girls of fifteen and women of thirty-five when pregnant have yielded positive results irrespective of the number of children born. In two cases, one pregnant and the other non-pregnant, in which the laboratory and clinical diagnoses were at variance, the subsequent course of events has justified the former. Both white and colored women have yielded positive and negative reactions in accordance with whether they were pregnant or not. An eclamptic in the sixth month gave a weak but definitely positive reaction. As controls, healthy men, virgins, women past the menopause, and non-pregnant women in the child-bearing period have uniformly given negative results. Likewise many pathologic conditions—syphilis, including one case of tabes, tuberculosis, malignant growths (one a case of carcinoma of the cervix), all acute infections encountered, comprising typhoid fever, general septicemia, acute endocarditis, acute pericarditis, gonorrheal arthritis, phlebitis, and acute pelvic inflammatory disease—these at least have been uniformly negative.

Only by the observance of the added precautions here indicated has the as yet incomplete series of cases undertaken in this laboratory been confirmatory as to the reliability of the serum diagnosis of Abderhalden. On the other hand, with the exercise of these controls the most meagre equipment indicated here has been reliable in the accurate performance of the test, the results being in perfect accord with those reported by Abderhalden.

SEVEN CASES OF CERVICAL RIB, ONE SIMULATING ANEURYSM.¹

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OF the 7 cases of cervical rib here presented, 5 came under my observation at the Gouverneur Tuberculosis Clinic, 1 at St. George's Tuberculosis Class, and 1 is reported through the courtesy of another physician whose patient she is. In 6 of the cases the condition was discovered in the course of routine chest examination, no attention having been drawn to it by the symptoms recorded; the history of the seventh case suggests the diagnosis.

After the comprehensive articles on cervical rib published by

¹ Five of these cases were reported before the New York Society of Internal Medicine, April 26, 1911. The remaining two were subsequently admitted to my service at the Gouverneur Clinic.

Keen² in 1907 and Goodhart³ in 1909, it is needless to review the previous literature for a *resume* of the subject. In brief, it may be stated that cervical rib is a congenital anomaly which may be associated with other defects of development, chiefly of the central nervous system; or it may exist alone, the latter being usually the case. It is often attended with slight or no symptoms, and may then be discovered only in the course of systematic physical examination, by the *x*-rays or at postmortem. It is often found in conjunction with a scoliosis, usually of the cervicodorsal type, and it is not infrequently associated with a neuropathic diathesis. It is a much more common condition than was formerly supposed, a large number of cases having been reported during the past fifteen years, after attention had been drawn to the subject, and especially since radiography has been available for diagnosis.

Although the existence or possibility of this condition was known to early authors, the first paper published on the subject was that of Hunauld,⁴ which appeared in 1742. In 1869 Gruber⁵ published a compilation of the recorded cases; but in 1875, one hundred and thirty-three years after Hunauld's description of cervical rib, only 79 cases had been reported, and of these only 5 were recognized during life. In 1894 the number of reported cases had increased to 139, of which 9 were diagnosticated in the living subject.⁶ In 1904, 34 cases recognized during life had been reported, and many more discovered at autopsy or in the dissecting room. Since that date a large number of living cases have been reported, in nearly all of which the diagnosis was confirmed by *x*-rays. Up to the publication of Keen's article 43 of these cases had come to operation, and the surgical importance of the condition is there fully discussed.

Although cervical rib is congenital, the age at which it has been discovered ranges from intra-uterine life to advanced years. It is much more frequently found in females than in males, the proportion being variously stated as two or three to one. In about two-thirds of the cases the condition is bilateral. Single cervical ribs are about equally frequent on the two sides. The anomalous ribs usually develop from the seventh cervical vertebra, more rarely from the sixth, and in only one known case from the fifth. Two cases have been reported in which there were two supernumerary ribs on one side.⁷

² AMER. JOUR. MED. SCI., 1907, cxxxiii, 173.

³ Ibid., cxxxviii, 666.

⁴ Mém. math. et phys. d. l'acad. r. d. sc., lvii, 1742.

⁵ Ueber die Halsrippen des Mensch, St. Petersburg, 1869, Mém. de l'acad. imp. d. sci., vii, Series 13, No. 2.

⁶ Pilling, Inaugural Dissertation, Rostock, 1894.

⁷ "In certain rare cases, accessory ribs have been observed in the lumbar region, but this anomaly is without clinical significance. There is no case on record in which a supernumerary rib had developed in both lumbar and cervical regions in the same individual." Goodhart, loc. cit.

The cervical ribs vary in length from a slight increase of the costal process of the vertebra to a complete rib united at its anterior extremity with the cartilage of the first dorsal rib. They may be flail-like,⁸ articulated, or immovable. The symptoms, when present, referable to the existence of cervical rib are of three groups—vasomotor, sensory, and muscular—and are due to the pressure of the bony tumor in the neck upon the subclavian artery and brachial plexus.

The principal vasomotor symptoms noted are visible pulsation of the subclavian artery, variations in the radial, brachial, or axillary pulses, gangrene of the fingers (rare), and edema, which is also rare, as the vein is seldom compressed. Sensory symptoms consist of pain, paresthesias, and disturbances of the tactile and temperature sense. Muscular symptoms of nerve origin include paresis, ataxia, and atrophy.

Actual paralysis has not been observed.

Two points of peculiar interest brought out in the literature of cervical rib are its frequent association with scoliosis and the late development of symptoms referable to the supernumerary rib. This latter fact has been variously attributed to growth of the individual, to trauma, to loss of flesh as a result of constitutional diseases, to arteriosclerosis, and to the retraction of the pulmonary apices in healed tuberculous lesions.

In all of the following 7 cases the cervical ribs were bilateral. In Case II, the supernumerary rib was apparently on the right side only, and in Case III on the left, but in both instances the *x*-rays revealed an undetected rib on the opposite side. In Cases VI and VII, both cervical ribs were rudimentary. In but 2 cases were any pressure symptoms reported, in both instances sensory, none showed any of the vasomotor phenomena, and but 1 the neuromuscular symptoms, described above. Six of the 7 cases were females.

The *x*-ray examinations of these patients were made by Dr. William H. Stewart, radiographer to Harlem and Gouverneur Hospitals, to whom I am also indebted for the plates and descriptions illustrating Cases II and III. I wish to make acknowledgment also of the courtesy of Dr. Henry E. Wise, in supplying the prints which accompany Case VI.

CASE I.—R. E., female, now aged twenty years; married; born in the United States. Her family history was negative. The previous medical history was not significant. She gave a history of influenza three times. It was shortly after her first attack, five years before, that she was sent to the Gouverneur Tuberculosis Clinic for examination. At that time she was pale, undernourished, and had a slight cough. She had no symptoms suggesting cervical

⁸ Francine, AMER. JOUR. MED. SCI., 1910, cxxxix, 108.

rib, but examination revealed prominent supraclavicular spaces on both sides, which on palpation seemed to be due to the presence of small bony masses near the cervical end of the fossæ. The percussion note over these masses was dull, and the breath sounds at the apices were distant, leading at first to the suspicion of tuberculous infiltration. The x-rays revealed the presence of double cervical ribs. The chest was otherwise negative, and the case was dismissed later as non-tuberculous.⁹ Now, after an interval of five years, the patient reports herself in good health. Since her discharge from the clinic she has married and has one child. Recently, however, there have developed some slight symptoms referable to the anomalous ribs. There is some impairment of the circulation in the right hand after prolonged use, manifested by a sensation of slight numbness, but without changes in color and without edema. She also complains of occasional pain "on top of the left shoulder."

The chief point of interest in this case is the presence of two well-marked cervical ribs occurring without symptoms of any kind until the patient reached the age of twenty, but giving rise to physical signs at the apices which suggested pulmonary tuberculosis.

CASE II.—A. K., female, aged sixteen years; Russian; occupation, milliner's trimmer. Her family history was negative. She had a personal history of measles and muscular rheumatism. About one year ago, she complained of slight cough and progressive weakness. She had been well previously, though overworked and living under unhygienic conditions. Several months after the beginning of her illness she was obliged to stop work because of weakness and dyspnea, and about this time she applied to the Central Health Department Tuberculosis Clinic for examination and treatment. She was there under observation for a time, and was discharged as not tuberculous. In July, 1910, she was sent into Gouverneur Clinic for examination through the courtesy of Dr. Charlotte Blum of the clinic staff, with the diagnosis of chronic endocarditis and aneurysm of the right common carotid artery. Physical examination revealed a small pulsating tumor, well above the inner end of the right clavicle. Percussion was flat over this mass and impaired at the outer end of the supraclavicular space. A distinct thrill and pulsation, which seemed to be expansile, could be detected on palpation, and on auscultation there was a loud systolic murmur synchronous with the apex beat and radial pulse. There was little if any difference between the right and left radial pulse. On deep palpation the pulsating tumor seemed to be superimposed upon a hard immovable mass of bony

⁹ This case, illustrated by x-ray plates taken at Hudson Street Hospital, was shown at the Practitioners' Society April 6, 1906, by Dr. Lewis A. Conner, and reported in the proceedings of the Society, Medical Record, lxi, 19.

consistency, which could be traced backward to the spine. Further examination of the chest revealed the characteristic signs of chronic endocarditis (mitral regurgitation), in a stage of incomplete compensation, to which could be attributed the dyspnea, cough, and weakness of which the patient complained. The lungs were negative. The patient was sent into the wards of Gouverneur Hospital, with a diagnosis of endocarditis and of right cervical rib with the

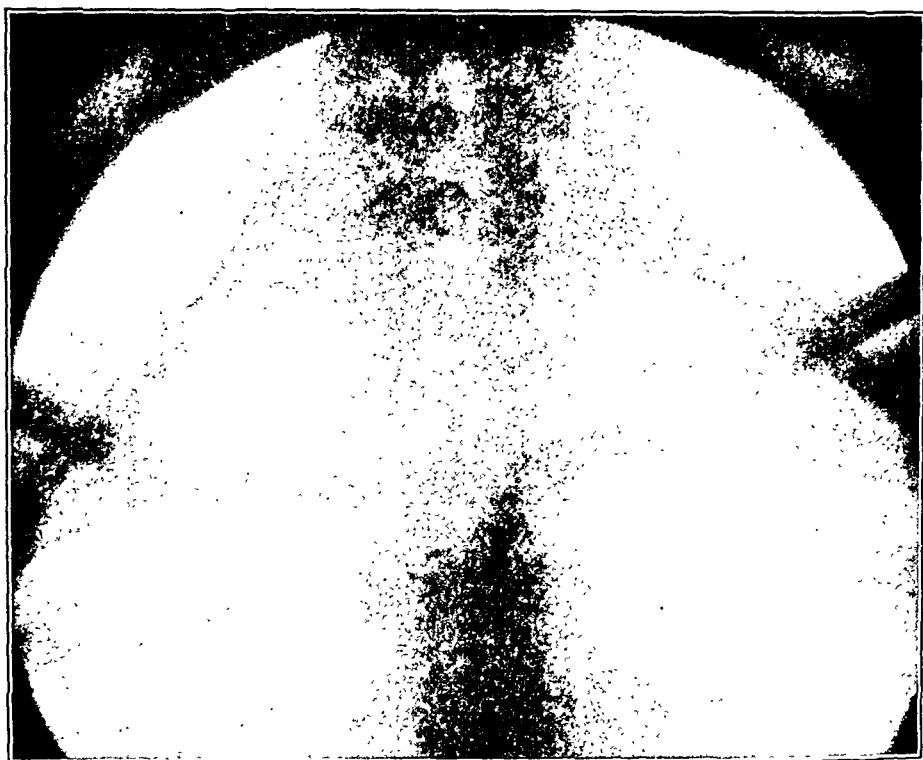


FIG. 1.—Radiogram of Case II. Right side: A well-marked cervical rib, with good head, articulating with the body of the seventh cervical vertebra. The neck, about one-half inch long, ends in a well-formed tubercle. The body broadens, then contracts, extending slightly downward for about an inch, ending in a club-shaped mass, which articulates with the first rib. The slight depression in the rib indicating the position of the artery and the shadow of the vessel itself are more apparent in the plate than in the reproduction. Left side: A rather long cervical rib with an ill-defined head and neck. A large tubercle, which articulates with the transverse process of the seventh cervical vertebra. A slender body about two and one-half inches long ending free.

subclavian artery overlying it at an angle simulating aneurysm. This diagnosis was confirmed by two x -ray examinations, one taken shortly after the admission of the patient to the hospital and the other several months later. The x -rays further revealed an undetected cervical rib on the left side.

This case is notable because of the position of the subclavian artery in relation to the anomalous rib and the consequent clinical resemblance to aneurysm, for which it had been mistaken. A

similar case is described by Osler,¹⁰ and the question of the existence of true aneurysm in these cases is discussed at length by Keen.¹¹ Keen believes that in few of these cases true aneurysm will be found at operation or postmortem examination, although several have shown moderate enlargement of the artery, curiously enough distal to the angulation or compression of the vessel, rather than proximal to the obstruction as might be expected. In a case reported by Murphy the artery was flattened. In a case reported by Adams an autopsy disclosed a true cylindrical aneurysm.



FIG. 2.—Radiogram of Case III. This patient has two well-formed cervical ribs, one on each side. They both have small heads with good necks, tubercles which are well developed, both articulating with the transverse process of the seventh cervical vertebra. The bodies are about one and one-half inches long, tapering toward the middle as they extend downward and outward, and ending in club-shaped masses lying near the first rib.

CASE III.—C. F., female, aged twenty-nine years; unmarried; born in the United States. Applied for examination at St. George's Tuberculosis Class in February, 1911. Family history negative. Past history of measles and pertussis in childhood. She had pleurisy nine years ago, with an attack of "bilious fever" (probably tuberculosis). Two years before this patient had been sent to Stony Wold Sanatorium in the Adirondacks for incipient pulmonary tuberculosis in the right apex. She was under treatment there for one year, and was discharged as an arrested case. Shortly after her return from the mountains she was operated upon for appendicitis. Since

¹⁰ AMER. JOUR. MED. SCI., 1910, cxxxix, 469.

¹¹ Loc. cit.

that time she has been in apparently good health. There have been no symptoms referable to cervical rib. She came to St. George's Class solely for observation of her lung condition. Physical examination revealed a prominent bony mass in the left supraclavicular fossa, which percussed flat and obscured the underlying apical resonance and breath sounds. A diagnosis of left cervical rib was made, which was subsequently confirmed by *x*-rays, the plate revealing also a right cervical rib. Signs of a healed lesion at the right apex were the only other findings on physical examination. The spine was negative.

This case is chiefly interesting for the size and prominence of one cervical rib, with an entire absence of pressure symptoms. In this case there had been a tuberculous process in the apex, but on the side of the unrecognized rib, and possible retraction of the apex following healing, if such occurred, gave rise to no symptoms.

CASE IV.—B. S., female, aged thirty-two years; married; housewife. Born in Russia. She was brought to me in March, 1911, by Dr. William Narins. She had been under his observation for some time previously, and was a case suspected of pulmonary tuberculosis with double cervical ribs. The family history was negative. The patient's previous history was suggestive of tuberculosis. She had had several slight attacks of hemoptysis. Physical examination showed prominent supraclavicular fossæ, with dulness on percussion and distant breath sounds. Small masses of bony consistency could be felt at the inner portion of the spaces. No definite signs of tuberculosis could be elicited at this examination. The *x*-rays revealed small double cervical ribs.

It has not been possible to secure this patient for further observation, but she gave no signs of compression and reported no symptoms which could be attributed to the supernumerary ribs.

CASE V.—E. L., female, aged forty years; single; stenographer; born in England. Her family history is suggestive. A brother died of "tuberculosis of the spine," and one uncle died of "tuberculosis of the intestines." Her personal history dealt chiefly with several attacks of "rheumatism" in 1903, 1905, and 1907. In the first two of these attacks the joints of the hands and knees were involved. The third attack, five years ago, affecting the right shoulder, was also diagnosticated as rheumatism. In October, 1909, she complained of some disability and pain in the right shoulder and arm, for which she was treated from October, 1909, to March, 1910, without improvement. Later she was told that she was suffering from neuritis, for which she was treated from March to September, 1910, with no better result. Since then she had had no definite treatment for the pain and weakness in the arm, from which she still suffered at intervals, especially after prolonged work. She complained also of some numbness and tingling in the right arm and hand, and found that this hand was easily fatigued.

Physical examination was facilitated in this case by the thinness of the patient, all the bones of the chest being unduly prominent. On inspection the veins of the chest were marked, and there was an evident mass at the inner end of the right supraclavicular fossa with a corresponding depression at its outer extremity. The mass was of bony consistency, immovable, and could be traced backward toward the spine—the familiar characteristics of cervical rib. Further examination of the chest showed extreme prominence of the lower dorsal spines, without other evidence of spondylitis, and of the coccyx. The lungs were negative save for a slight increase in breath and voice sounds at the right apex, not positively beyond physiological limits. The heart was normal.

This case was evidently recognized by some previous observer, as the patient said she was examined several years before with the *x*-rays (fluoroscopic), and was told at that time that she had an "extra rib" which would never give her any trouble. No operative procedure was suggested to her then, or since.

I am enabled to report this case through the courtesy of Dr. Rose Cohen, who saw the patient recently in private practice. The points of special interest are the development of slight but characteristic symptoms at the age of thirty-eight years, and the possible co-existence of healed tuberculous foci in the right pulmonary apex and the lower dorsal vertebræ, suggested by the physical examination taken in connection with the family history.

The *x*-ray examination of this case, made by Dr. Stewart, showed double cervical ribs, the right being the more prominent.

Cases VI and VII were both admitted to my service at Gouverneur Tuberculosis Clinic within the past year. For the reproductions of the *x*-ray plates, I am indebted to Dr. Wise, radiographer at Gouverneur Hospital.

CASE VI.—J. S., male, aged twenty-four years; operator; Russian Hebrew. This patient was sent to the Clinic by the United Hebrew Charities Society on the suspicion of pulmonary tuberculosis. His family history was negative, and his personal history was without significance. Five months before admission to the clinic he complained of vague pains in his chest, and later, pains in his legs, weakness, and headache, a familiar group of symptoms in this class of patients. A slight loss of weight during the three weeks he was under observation at the clinic, and the tendency to rapid pulse, were more suggestive. On examination of the chest the patient was seen to have a fairly well-marked right dorsal scoliosis and prominent supraclavicular spaces, in which, upon palpation, the characteristic bony masses suggestive of cervical rib were detected, the left being more prominent than the right. Examination of the lungs showed impairment of both apices, more marked on the right side, with roughened breathing,

but no rales. The heart was negative. Sputum negative. A diagnosis of double cervical rib was confirmed by x -ray examination.

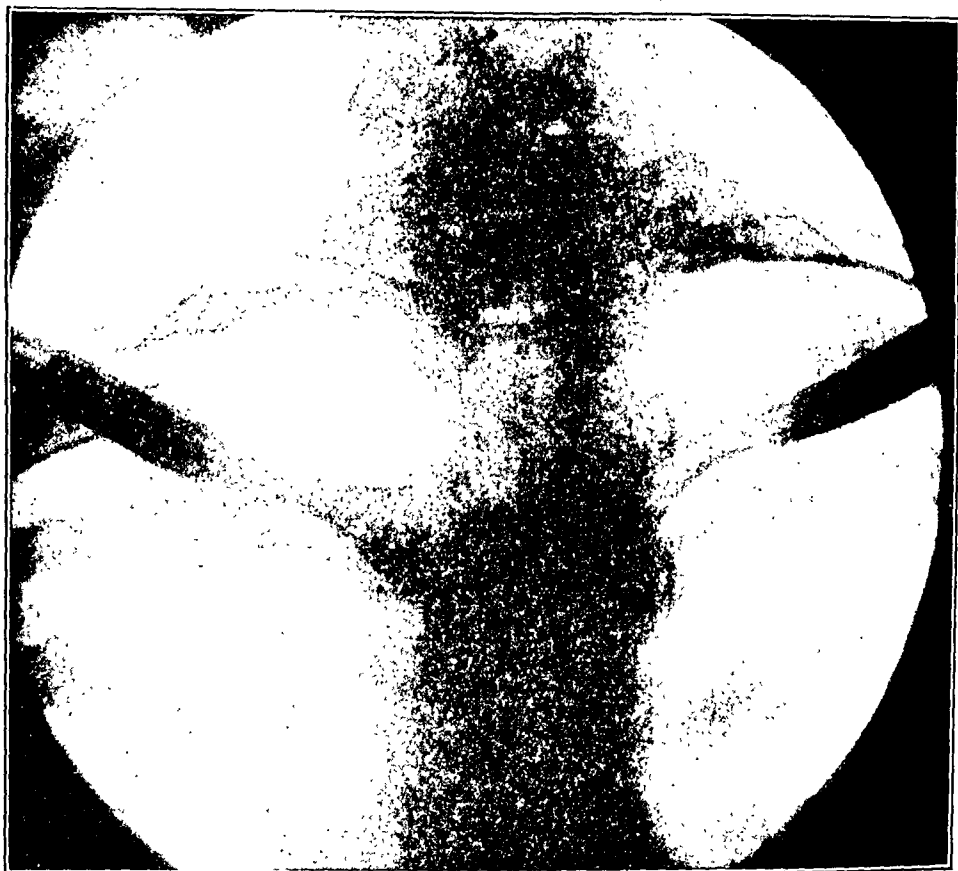


FIG. 3.—Radiogram of Case VI.

This case was the only male in my series. Like all but one of the series, he was examined on the suspicion of pulmonary tuberculosis, and while the physical findings were suggestive only of a healed lesion or inactive process at the apices, the period of observation was too brief for final diagnosis. It is the only case in the series showing well-marked scoliosis. There were no symptoms referable to the supernumerary ribs.

CASE VII.—B. B., female, aged eighteen years; operator on garments; Russian Jewess. She was referred to us by a physician in the district, with the diagnosis of consumption. This diagnosis was confirmed by physical examination. The sputum was also positive. She was an early case, showing only impairment of resonance at the apices with little change in breath sounds and occasional clicking rales after expiratory cough. It was noted, however, that the supraclavicular spaces were prominent, and that the impairment of resonance which corresponded to these areas

was out of proportion to the other pulmonary signs. A diagnosis of double cervical rib was later confirmed by *x*-rays. There were no symptoms referable to the condition, nor have any such developed during the eight months she has been under our observation. She is, however, a progressive pulmonary case, and has recently been sent to a sanatorium. The spine in this case was negative.

In reviewing the cases of cervical rib here submitted, it will be noted that in six of the seven cases pulmonary tuberculosis had been suspected, but that only two of them showed positive signs of the disease (Cases III and VII), and that in only one of these (Case VII) was it an active process. Cases IV and VI were suspicious, but were not under observation long enough for a final diagnosis of the pulmonary condition. Case V may have had a healed tuberculous lesion at the right apex, but it was exceedingly doubtful from the physical signs, and this was the only case with pressure symptoms. Two cases were definitely not tuberculous. One was the cardiac case with physical signs simulating aneurysm (Case II), the other (Case I) was dismissed as entirely negative, and now, after an interval of six years, is still in good health, although recently having slight pressure symptoms on one side. Well-marked scoliosis was observed in only one of the series (Case VI), and that one is the only male of the group.

Only two of the series have presented any symptoms referable to the presence of cervical ribs (Cases I and V), and only the latter of these has suffered any real disability. The symptoms in this instance are apparently due to pressure upon, or stretching, of the lower branches of the brachial plexus, there being no apparent vasomotor disturbance, and in this case only does the question of operative procedure suggest itself. Incidentally this patient is the oldest of the group, and the symptoms in her case did not develop until her thirty-eighth year.

In three instances a diagnosis of unilateral cervical rib was made clinically, but in these, as well as in those cases in which a double rib was detected, the *x*-rays revealed bilateral processes.

In conclusion, the following statements seem to be justified, in summarizing our present knowledge of cervical rib, from the mass of previous evidence as well as from the cases here reported:

1. Cervical rib, especially of the bilateral type, is not of great rarity, probably occurring much more often than it is recognized.
2. It may be recognized clinically in the course of a systematic physical examination, especially in a thorough examination of the chest for pulmonary tuberculosis, and even when there have been no symptoms which might direct the attention of the clinician to the possibility of the condition; but a positive diagnosis of cervical rib cannot be made with certainty without the *x*-rays.
3. The condition is found much more frequently in females than in males, and is often associated with scoliosis; it is not infre-

quently accompanied by pulmonary tuberculosis, although this latter coincidence seems to be without clinical significance except in diagnosis.

4. Cervical rib may occur without symptoms, or with symptoms so slight as not to constitute any inconvenience or disability; and this may be true even when the cervical rib is of unusual size or prominence, as in several of my series.

5. Symptoms may develop at any age, and with or without a history of injury, occupational strain, or other known etiological factor, but they are much more apt to develop later in life and without definite history of causation.

6. In certain cases of cervical rib the abnormal course of the subclavian artery may simulate aneurysm, but true aneurysm is probably infrequent in these cases, and can only be demonstrated by operation or at autopsy.

7. In those cases presenting symptoms of sufficient severity to warrant operation, the resection of the supernumerary rib under recent technique offers every reasonable prospect of complete recovery.

8. In some cases of cervical rib the only clinical significance which can be attached to the condition lies in the fact that the recognition of early pulmonary tuberculosis may be rendered difficult through the presence of the supernumerary rib obscuring definite signs at the apex underlying it; or, of equal importance, that the presence of cervical rib in some cases of suspected tuberculosis may lead to a mistaken diagnosis of apical lesion because of the confusing signs above the clavicle due to the presence of this anomaly.

THE POLYNEURITIC FORM OF ACUTE POLIOMYELITIS: A CLINICAL AND PATHOLOGIC STUDY.

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THE question of the existence of a true polyneuritic form of acute poliomyelitis has never been satisfactorily determined. As far as I am aware no case has ever come to necropsy. Wickman in his article on "Acute Poliomyelitis" in Lewandowsky's *Handbook*, published in 1911, states "that he was unable to find in the literature a report of this type in which the peripheral nerves had been studied." Recently, I had the opportunity of studying a fatal case under the care of Dr. Pitfield.

A. S., female, aged twenty years, was admitted to the hospital on August 17, 1911. Nothing of importance was noted in the family or medical history. Her illness began several days previous

to admission with nausea, vomiting, and fever, accompanied by severe pain in the back of the head and neck. A few days later pains and paralysis occurred in both lower limbs, especially the left. Physical examination of the heart and lungs showed no changes. The abdomen was somewhat distended.

The left lower limb was completely and the right lower limb was partially paralyzed, and only the foot could be moved. Pain on pressure over the nerve trunks was noted in both limbs. The left knee-joint was swollen. There was paralysis of the bladder.

No changes were found in the urine. The blood examination showed: Red blood cells, 4,600,000; white blood cells, 7200; hemoglobin, 80. The Wassermann reaction was negative.

August 29. General condition as on admission, save that the patient voids urine voluntarily.

September 18. Pupils equal; reacted to light and accommodation. There were no ocular palsies. The eye-grounds showed no changes. There was no involvement of the cranial nerves. She could move either arm freely, and in all directions. The biceps-jerk was normal. There were no sensory disturbances in the arms or hands. She could move the right foot and leg slightly. The left limb could not be moved at all. Both patellar tendon reflexes were absent. The knee-joints were swollen. Tactile sensation was diminished in both lower limbs. A pin-point was felt over the entire left lower extremity, but not so distinctly over the right lower limb above the knee. There was marked tenderness over the nerve trunks in the lower limbs.

September 24. The urine showed casts and albumin. The condition of the patient remained the same, except that the temperature rose on the thirty-third day, and remained between 102° and 104° until death.

HISTORY. A young adult female, without any previous illness, was suddenly seized with vomiting, fever, pain in the head and back, followed in several days by pain and paralysis in the lower limbs, together with paralysis of the bladder. The important physical symptoms were loss of patellar tendon reflexes and unsymmetric paralysis of both lower limbs, with partial areas of hypesthesia. There was bladder paralysis. In addition there was marked tenderness on pressure over the nerve trunks in the paralyzed extremities; which persisted until death, two months after the onset.

At necropsy the heart, lungs, spleen, and liver showed no changes. The kidneys showed cloudy swelling. A few punctate hemorrhages were seen in the visceral pericardium.

No exudate was noted in the meninges of the brain or spinal cord. The vessels were injected. The cord in the lumbar region was somewhat softer than in the other portions, and on section showed a reddish-gray area in both anterior horns.

Microscopic sections were made from various levels of the spinal cord and medulla oblongata. These sections were stained with thionin hemalum and acid fuchsin, by Weigert's stain, and by the Marchi stain.

Only one peripheral nerve and portion of one muscle were obtained and these were from the anterior aspect of the right thigh, near Poupert's ligament. A portion of the nerve was placed immediately in osmic acid and teased after twenty-four hours. Another portion was placed in Müller's fluid and studied by the Weigert, hemalum, and acid fuchsin stains. There was no evidence of an acute or subacute inflammatory process, and no distinct degenerative changes were noted. The hemalum-acid-fuchsin stain showed slight increase in the connective tissue. There was no round-celled infiltration. The osmic acid showed slight swelling of the fibers, some granulation of the myelin, but no breaking up into droplets. Most of the fibers were normal with Weigert's stain.

The section of muscle showed no round-celled infiltration, no swelling or atrophy of fibers. The striations could be seen, but were not sharply defined.

In the medulla oblongata no changes were noted.

The cervical and thoracic areas of the spinal cord showed no changes.

In the lumbar area stained with the hemalum-acid-fuchsin the meninges showed an intense round-celled infiltration.

The pial vessels were dilated and intensely engorged with blood. Around and within the anterior and posterior roots the round-celled infiltration was intense, and the capillaries were intensely dilated.

The anterior horns showed the characteristic picture of the subacute stage of an acute poliomyelitis.

The left anterior horn was more involved than the right. The capillaries were injected, the round-celled infiltration was marked, and the cells showing a clear protoplasmic area around the nucleus.

Many lymphoid cells, a few connective-tissue and polymorphonuclear cells were also seen. The ganglion cells had practically disappeared as only a few were seen, and those remaining were atrophied. With the Nissl stain the disappearance of the ganglion cells and the varying grades of degeneration of those remaining were most marked.

No changes were seen in the posterior horns or in the white matter. The Weigert stain showed no sclerosis.

These changes were noted in the second, third, fourth, and fifth lumbar segments.

PATHOLOGIC HISTORY. The changes found in the lumbar region of the spinal cord were those of an acute poliomyelitis in the reparative stage.

The anterior horns were practically destroyed. Intense inflammation was noted in the meninges and around the posterior roots.

Most interesting was the exudate and inflammation of the spinal roots.

The peripheral nerve showed no evidence of a primary neuritis, and the changes present were probably secondary in character.

The diagnosis of this case was difficult. The possibility of a true multiple neuritis had to be excluded. Pain on pressure over the nerve trunks, which is emphasized so much in text-books, could not be considered as a differential symptom.

True multiple neuritis develops slowly, fever is usually absent, special groups of muscles are affected, and the distribution is more symmetric. The absence of sore throat and any history of diphtheria precluded a diphtheritis neuritis, the paralysis in this also occurs much later than the throat disorder; a neuritis of other type, could not with certainty be excluded. The diagnosis of the polyneuritic form of acute poliomyelitis was substantiated by the presence of several other cases in the same vicinity, the unsymmetric involvement of the paralysis, and the absence of cranial nerve involvement, though there are cases of multiple neuritis in which only the spinal nerves are affected, and cases of acute poliomyelitis have been reported with cranial nerve paralysis.

The resemblance of multiple neuritis to poliomyelitis has been known ever since Leyden recognized a clinical relationship.

This similarity in the clinical pictures of the two diseases was recognized in the chronic form of the spinal disease, but recent studies have established the resemblance to acute poliomyelitis.

Cases were described clinically by Strümpell and Barthelmes in 1900. Wickman in 1905 reported a few cases, and in the epidemics observed by Hartman, Foerster, Müller, Mills, and Spiller this form has been recognized. In Foerster's cases everyone showed pain and tenderness on pressure over the nerve trunks, which continued for months. At least clinically there seems to be no question of a polyneuritic form. These cases are remarkable in the prominent part played by the pain over the nerve trunk. After a shorter or longer interval, varying from days to several months, this pain disappears. These cases may recover completely or show permanent paralysis; in rare instances they are fatal.

Those cases in which the pain resolves itself into a hyperesthesia of the skin or on movement of the joints or limbs should not be included in the polyneuritic form. Many cases of acute poliomyelitis may show this at the onset of the disease.

In some of the polyneuritic forms, objective sensory symptoms may be present, such as hypesthesia and disturbances of pain and temperature.

Pathologic evidence of this form is wanting. The peripheral nerves have never been examined in any such case. Cases of acute and subacute poliomyelitis not of the neuritic type have been reported in which the peripheral nerves were studied. In the cases of Redlich, Monkberg, Mott, and others the nerves were

found degenerated. This degeneration could be attributed to a secondary change, owing to the long duration of the cases (from thirteen days to several months).

Harbitz and Schell's cases of acute poliomyelitis, with pain, do not answer to the polyneuritic type, though their findings are of interest.

In their Case VI, a boy, aged six years, had headache, pain in the neck, and pain in the arms. Examination of the brachial plexus and the vagus nerve showed no inflammation or degeneration.

In their Case VIII, one of poliomyelitis, with bulbar symptoms, in which pain played a prominent part at the onset, the vagus, phrenic, and cervical plexus showed no changes.

Their Case X showed an acute onset, with headache, fever, pain in the limbs, and bladder paralysis. No changes were noted in the peripheral nerves.

Wickman believes that the peripheral nerves are never involved and that the pain is due to the meninges, while Raymond held the view that the whole peripheral neuron is affected.

Strümpell, while admitting the involvement of the peripheral neuron, believes that the two diseases are distinct, in that in the spinal type we are dealing with a focal lesion, while in the neuritic form we have the effect of a toxic disturbance in the general circulation.

The pathologic evidence was wanting of any primary degeneration of the peripheral nerve in my case. There were no inflammatory changes. That only one nerve was studied renders this evidence insufficient, but it is reasonable to assume that even this should have shown some neuritis.

Changes may, however, be absent even in true neuritis. Spiller has examined the nerves in different cases of peripheral neuritis, and in some instances he has failed to find any change. This he attributes to the unequal distribution of the inflammatory process, though clinically in his cases the pain was felt along the entire nerve. The more central portions of a nerve may escape when the peripheral portions are diseased. Swelling of the nerve at one portion would produce pain throughout, yet the nerve above the swelling might not show any changes.

Pathologic evidence was not lacking to explain the pain in the case reported. The intense inflammation in the meninges, quite marked around the posterior roots, and the swelling of these roots, on account of the exudation of the round cells within them, as well as the intense engorgement of their vessels, might well account for the pain. The tenderness along the nerve trunks could easily result from this central irritation. In this connection it would be interesting to know whether in other diseases of the spinal cord such as tumor, etc., in which the spinal roots are irritated, tenderness could be elicited along the nerve trunks. That it occurs usually in acute meningitis is well known.

AN INTENSIVE STUDY OF INSECTS AS A POSSIBLE ETIOLOGIC FACTOR IN PELLAGRA.

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IN 1911, Dr. J. W. Babcock, Superintendent of the State Hospital for the Insane at Columbia, South Carolina, brought to the attention of the State authorities, the desirability of an investigation into prevalence and etiology of pellagra.

Following this action, through the initiative of Dr. J. A. Hayne, Secretary of the State Board of Health and Representatives A. F. Lever and Joseph T. Johnson of South Carolina, the writers were, early in 1912, assigned by Dr. L. O. Howard, Chief of the Bureau of Entomology, United States Department of Agriculture, under the direction of Mr. W. D. Hunter, of the Bureau, to investigate the possible relation of insects to pellagra and to gather such data as might serve to indicate whether there was ground for the assumption that blood sucking or other arthropods were involved in the transmission of pellagra in South Carolina.

After several months' work in various parts of the State, we were afforded opportunity to coöperate with the Thompson-McFadden Pellagra Commission of the Department of Tropical Medicine of the New York Post-Graduate School upon its arrival in Spartanburg County. From June 15 until the middle of October, our own studies were carried on in Spartanburg County in collaboration with this Commission, and it is with this portion of our field work that the present preliminary report has to deal.

These studies included the investigation of the premises of pellagrins and of the neighborhoods in which they resided, with special reference to the presence, distribution, and biologies of such insect groups and species as appeared worthy of consideration, after careful study of the conditions.

To this end, we visited the houses of as many as possible of the cases studied by the Commission, and made minute observations of the insect fauna. The patients and their families were questioned in order to obtain such histories as they could give of the attacks or presence of insects and their general experience in regard to the pests with which they were familiar. In many instances the houses were visited more than once, and comparative observations were made under varying conditions. In some instances, the studies were extended to the homes of the non-pellagrous inhabitants of mill villages and elsewhere and the data thus gathered were used to

confirm and extend the information obtained from the patients themselves. Sanitary and other conditions which might have a bearing upon the presence or abundance of insects were noted, and the more remote surroundings were inspected and studied in connection with such forms of insect life, occurring in such situations, as might influence the pellagra focus under investigation. When this focus was of considerable importance, with marked incidence of the disease, the neighborhood, as a whole, was investigated comprehensively and all possible facts bearing upon the situation were noted.

As a rule, the persons interviewed were ready to give such information as they possessed regarding the insect pests with which they came in contact. It was fully realized that popular observations of this nature are liable to be highly inaccurate. Great care was therefore exercised in making the inquiries and in sifting the information obtained. Only such reports were recorded as gave evidence of reliability and clearly referred to the insect which was the subject of the inquiry.

The breeding of certain insects was attempted, but owing to the character of the available facilities and the exactions of the active field work, but meagre results were obtained. This phase of the investigation was therefore unavoidably subordinated to that of the entomological side of the general epidemiological study.

CHARACTER AND ECONOMIC CONDITION OF SPARTANBURG COUNTY. The following description of Spartanburg County and its climate is quoted from the preliminary report of the Thompson-McFadden Pellagra Commission:¹

"Spartanburg County is situated in the northern or Piedmont section of South Carolina. It is forty miles long in a north-south direction, thirty miles from east to west, and contains 762 square miles. Its surface is hilly and broken by a network of small streams and by four rivers which, with their tributaries, flow across the country in a southeasterly direction, one of these rivers forming the county line of the south. The elevation above sea level at Spartanburg, the county seat, is 875 feet. To the northwest, the slope is upward, the northwest corner of the county being situated at the foot of the Blue Mountain range, while to the south and east the elevation becomes somewhat lower than at Spartanburg, but with no precipitate fall, the whole county thus resting upon a plateau over 700 feet above sea level."

There are no considerable swamps or marshes, and small areas of boggy ground in the neighborhood of streams, while not uncommon, were generally found to be negligible in connection with the breeding of insects of economic importance.

"The annual mean temperature, as recorded at Spartanburg, is

¹ Epidemiological Studies, Part I., AMER. JOUR. MED. SCI., July, 1913, pp. 44-45.

60° F. While the winters are mild, killing frosts are apt to occur from November to March inclusive, and the normal mean temperature for the months of December, January, and February is about 42° F.

"The total population of the county is 83,465. Spartanburg, with a population of 17,517, is the only city in the county, the remaining population (65,948) being distributed on farms, in cotton mill villages, and among eleven small towns, only two of which have over 1000 inhabitants. The density of population, as a whole, is 109 per square mile; for the rural population (*i. e.*, outside of Spartanburg City), it is 86.5. While in South Carolina, as a whole, the negroes form 55 per cent. of the total population, in Spartanburg County the whites predominate numerically in the proportion of somewhat over two whites to one negro, there being a white population of 57,055, and 26,410 negroes, the percentage being 68.4 per cent. whites, and 31.6 per cent. negroes."

"The chief industry, and almost the only industry conducted upon a large scale, is that connected with the cotton mills. There are twenty-eight cotton mills in the county, each mill supporting its own village. These mills give employment to approximately 10,000 operatives, representing about 4000 families, and a total mill-village population of about 20,000."

EPIDEMIOLOGY. The epidemiology of pellagra in Spartanburg County presents certain features which have a distinct bearing upon the subject of insect transmission, and may be briefly summarized.

The cases considered in this report are distributed among the population as follows: Mill, 151 cases; rural, 77 cases; and urban, 51 cases.

Divided according to sex, there are: Male cases 71, or 25 per cent., female cases 211, or 75 per cent., or three females to one male.

These are distributed as follows: Mill cases, males, 38; females, 113. Rural, males, 19; females, 58. Urban, males, 11; females, 40.

The racial distribution shows 257 cases among the whites to 25 among the negroes, a ratio of 10 to 1.

The economic condition of the cases may be thus summarized: 85 per cent. were in poor circumstances; 15 per cent. were comfortable; and 2 per cent. were affluent.

The age of the males and females affected is shown as follows: Under five years, 21; five to nine years, 22; ten to nineteen years, 28; twenty to forty-four years, 158; and over forty-four years, 53.

By sex and age, cases appear as follows: Under five years, males, 10; females, 11. Five to nine years, males, 12; females, 12. Ten to nineteen years, males, 7; females, 16. Twenty to forty-four years, males, 16; females, 148. Over forty-four years, males, 25; females, 27.

SEX INCIDENCE. The sex incidence presents striking features. As shown above, the proportion of female to male cases is 3 to 1; and statistics for the entire endemic area in the United States show that this is the approximate ratio throughout.² So pronounced an inequality must be based upon some fundamental difference either in environment or physiologic organization of the sexes. It is difficult to account for the inequality upon the ground of great female susceptibility, as such susceptibility is contrary to medical experience and to the well recognized natural law that the female in general is more resistant to adverse influences than the male. Cases of pellagra originating in institutions for the insane have also shown an approximately equal distribution among males and females.³

Beall⁴ has sought to explain the inequality in sex incidence by associating the immediate cause of pellagra with the dwelling, calling attention to the high rate among females whose time is largely spent about the home, and to the fact that a large proportion of the male cases occurs during the ages when the association with the home is closest, that is, among children and the aged; men during their active years escaping to a great degree.

Of the 282 cases studied, 211, or 75 per cent. were females, of whom 173 were adults; and of these adults, 142, or 82 per cent. were engaged in housework most or all of the time. The adult female population of the mill villages, divided between mill operatives and those who devote themselves mainly or exclusively to household occupations, afforded an opportunity to compare two classes living under seemingly identical conditions with the exception of those of occupation. Of this class, there were 88 female cases, of whom 60 cases, or 68 per cent., gave all or most of their time to housework; the remaining 28 women, or 32 per cent., were engaged in mill work for a portion or all of their time. This disparity, marked as it is, becomes more striking when only those engaged exclusively in house or mill work are compared. Here we find but 12 cases among those who work in the mills, while 46 women, who were occupied exclusively with housework, were affected, the percentages of these groups being 13.6 and 52 respectively. Thus it is seen that a close correlation appears to exist between pellagrous incidence and the amount of time spent in or about the home, and that this holds, not only when the sexes are compared, but within the sexes, themselves. 12-1

A marked characteristic of pellagra in all countries is its rural nature. Although the disease sometimes appears to originate in

² S. A. Roberts, Pellagra, St. Louis, 1912. K. H. Beall, Bull. Texas State Board Health, 1911, v, No. 9. Tennessee State Board Health, Report on 316 Cases of Pellagra, 1911. C. H. Lavinder, Reprint from P. H. Rep. 65, 1911. R. M. Grimm, P. H. Rep., 1911, xxvi, No. 38.

³ H. Douglas Singer, Report Pellagra Commission, State of Illinois, 1911.

⁴ K. H. Beall, Loc. cit.

cities of considerable size, an analysis of conditions in such cities will usually, if not always, show that in certain important aspects, the rural element governing the presence and abundance of insects is predominant.

Isolated sporadic cases of a disease are highly suggestive of an insect carrier, under certain circumstances, especially when exposure of the individual to infection by association with other cases may be excluded. The suggestiveness is strengthened, in the case of pellagra, by the existing evidence against direct contagion and also by the low degree of infectiousness which the disease appears to exhibit.

Another fact which may point to the agency of an insect in pellagra transmission, is the occurrence of several cases in a single family, and this frequently happens. It is obvious that the close association of persons constituting the household would increase the opportunity for transmission by predatory insects. This feature is emphasized by what appears to be a definite chronological connection between such cases.

At the same time, the large number of instances in which but a single member of a household is affected, does not preclude the same possibility. It is conceivable that by reason of habits or constitution, the unaffected members, might, for a time, altogether escape infection. Or, scarcity of the insect carriers, especially if conditions favor their free entrance into and departure from the house, may lessen the chances of transmission within the home.

Attention may be directed to some features of the epidemiology of pellagra which suggest a certain analogy to those of two other diseases, viz., malaria, an insect-borne protozoal disease often of chronic character; and acute anterior poliomyelitis, which, as apparently shown by certain recent experiments, may be transmitted by biting flies, thus strongly indicating at least one of the channels for the communication of that disease.

The seasonal recurrence of pellagra and its period of greatest development during the summer months, the period of greatest insect activity, finds an approximately similar condition in malaria and probably a greater similarity in the case of poliomyelitis. Both of these diseases are largely of rural origin, as is pellagra. Poliomyelitis, moreover, is marked by the occurrence of sporadic cases, not to be explained by contact infection and there is a lack of evidence of direct contagion, two facts which are true of pellagra.

THE INSECTS STUDIED. While the object of our investigation was the study of all insects which may have any part in the transmission of pellagra, it was realized that a careful consideration of conditions and of the insect fauna would inevitably narrow the field to a few genera and species. It became clear that efforts might safely be concentrated upon a few groups of insects, mostly of blood-sucking habits. Keeping in view the conditions which

are imposed by the facts of disease transmission by insects, the following groups were given careful attention: Diptera, or two-winged flies; Hemiptera, including the lice and bed-bugs; Siphonaptera, or fleas, and Acarina, or ticks. Some attention was also paid to the roaches, Blattidæ.

ACARINA. The ticks of the family Ixodidæ must be mentioned, although their importance in this connection is negated by their habits, life history and the infrequency with which the persons who suffer most from pellagra appear to come in contact with these arthropods in Spartanburg County.

It will be remembered that most ticks of the family Ixodidæ (no members of the family Argasidæ occur in Spartanburg County) require three hosts during their period of development, dropping to the ground on the completion of each stage and reattaching themselves to another host, sometimes of a totally different species, when they have advanced to the next stage of their existence. The chances of any tick of this group attaching to successive human hosts are remote. It is unusual for these parasites to remain undiscovered on man long enough to complete the stage during which attachment was effected. Almost certainly they are removed and killed and transmission of infection from the first host thereby prevented. The presence of animal reservoirs of infection would therefore seem to offer the only means by which this disease could be transmitted by the group of ticks mentioned and there is no indication that such reservoirs exist. Reports from pellagrins and non-pellagrins of attacks by ticks were rare and in the course of the work only two lots of ticks were collected, one lot from dog and one on the clothing of man. Many dogs and other animals were examined and the indication is that the tick infestation of the country is light. *Amblyomma americanum* and *Dermacentor variabilis* probably occur in the county. The usual hosts of these species are dogs but they are known to attach to man.

It is impossible to explain the sex incidence of pellagra by the incrimination of ticks, men being obviously more exposed to their attack than women. In view of this fact and the lack of evidence that animals are subject to and can serve as reservoirs of pellagrous infection, the almost certain death of all ixodid ticks which bite human beings, together with the equal certainty that not all pellagra sufferers in the region can have been exposed to the bites of ticks, these arthropods can safely be excluded from among the possible factors of pellagra transmission.

PEDICULUS VESTIMENTI AND CAPITIS. Head lice (*Pediculus capitis*) were locally said to be far from rare among certain classes of the population, but this statement is not borne out by our observations or by reports received. Only one or two reports of previous experience with the parasite could be obtained, and the writers saw but one case of actual infestation. As reports regarding such insects

as bed-bugs and fleas were usually frankly given, it seems hardly probable that reticence could account for the many negative reports in regard to *Pediculus*. We are forced to believe that whatever may be its prevalence, it is far from universal and entirely inadequate as a possible agent in the transmission of the disease. That a wingless insect with the habits and associations of the head louse can be the cause of infection in any but a very limited class of cases, is scarcely to be credited, and such an inference leaves the question of female preponderance and sporadic cases unsatisfactorily answered.

It is well known that head lice will, upon occasion, be transferred from infested to clean persons, but observations indicate that unless the infestation is gross or the association of persons is intimate such transfer of the parasite is not particularly common, and this is borne out by the experience of persons of ordinarily careful habits. We are unable to see that the head louse can be incriminated when we consider its rare occurrence upon persons of fastidious habits, who yet furnish an appreciable number of cases of pellagra.

No reports of *Pediculus vestimenti* were received and no observations of the species were made. The evident rarity of the species as well as its habits exclude it from consideration as definitely as the foregoing.

CIMEX LECTULARIUS. The bed-bug (*Cimex lectularius*) was found to be of practically universal occurrence in the houses of the largest class of pellagrins of the region. Of 256 reports received from pellagrins, the actual presence or recent attacks of bed-bugs were admitted in 241 instances. Only 15 persons denied that they had been exposed to this pest, and from their known prevalence in the mill villages and elsewhere some doubt may be entertained as to the accuracy of at least some of the negative reports.

Concerning the incrimination of *Cimex* in pellagra transmission, there is one fact which alone is sufficient to indicate its innocence. This is the sex incidence of the disease. It has never been shown that *Cimex* attacks females more frequently than males, certainly not in the proportion of 3 to 1, or if adults in the prime of life are considered, of 9 to 1. If this is not the case, the explanation of transmission by the insect is unsatisfactory. In the often crowded, badly infested, and none too cleanly homes of a considerable class of pellagra sufferers, indiscriminate attacks of the insect are greatly facilitated and must certainly be made upon the inmates without regard to age or sex.

It is well known that the bed-bug has the power to endure starvation for extended periods, and nothing is more difficult than eradication of the pest when it has once taken possession of a building. If it were capable of conveying pellagrous infection, these qualities might account for what has been termed the "place infection" of pellagra. At this time, proof is lacking of such a source

of infection, but should it be shown to exist, the facts of sex incidence just cited together with the occurrence of but one case in a family in many instances must stand opposed to incrimination of the insect.

While but 2 per cent. of the pellagra cases studied were in affluent circumstances, others of this class have come to our notice in other localities, and it may be asserted that such cases are by no means rare. It cannot be questioned that the habits of life and general associations of such persons greatly minimize the possibility of their infection having been brought about through the agency of the bed-bug.

Specimens of this species were collected in connection with some cases, but no special effort was made to do so in the majority of instances. No systematic search for a causative organism was being prosecuted nor transmission experiments carried on in the field. It was therefore considered that the value of actual collections of bed-bugs, systematically made, hardly justified the time required and the interruption caused to the routine pursued in securing case histories of pellagrins. In addition, the positive reports generally received, supported by occasional collections seemed amply sufficient to establish the almost universal presence of the pest.

BLATTIDÆ. Of roaches, only the common cockroach, *Periplaneta orientalis* and the smaller *Ectobia germanica* were encountered. These disagreeable household pests were found to be abundant and generally distributed, but nothing remarkable was noted in their relations to the homes of pellagra cases or of the population in general.

Though armed with strong, biting jaws which enable the insects to commit serious injury to leather and other substances there are few accounts in the literature of attacks upon human beings, and these seem to be confined to nibbling of toenails, eyelashes, etc. Even such as they are, attacks upon man must be considered exceedingly rare, and they cannot be considered a factor in transmission.

The well known habit of roaches of frequenting kitchens and larders, their omnivorous habits, and the inefficient protection of food too frequently practised by the classes who suffer most from pellagra suggest the possibility of its transmission by food contamination. If such means is possible the part played by the insects must be far less important than that of house flies, for the exposure of food to the latter is unquestionably greater and the carriage of fecal matter far more regular and constant than can be the case with roaches. Certain experiments conducted by one of us (A. H. J.) indicate that roaches will not readily feed upon such material and under normal conditions their opportunities for the

contamination of foodstuffs with human excreta are far less than those afforded house flies.

Roaches can, therefore, not be considered an important element in pellagra causation and must be considered in the same category with, but far inferior to, the house fly.

TABANIDÆ. Flies of the family Tabanidæ, which includes the well-known horse-flies, were rare in Spartanburg County during the season of 1912. One or two specimens of *Tabanus atratus* (?) were seen flying about our automobile while in motion, but none were captured. Only two specimens of Tabanidæ were collected in Spartanburg County and these were unfortunately lost before exact determinations were made. The flies of this group are primarily a pest of the larger domestic and also of wild animals in localities where the latter are found, and their habits are such as to exclude them from the possibility of an active role in pellagra transmission. In localities where Tabanidæ are numerous the biting of human beings is by no means uncommon, yet even in such regions bites are scarcely received with the frequency and regularity which are essential to the transmission of human disease in the absence of an animal reservoir of infection.

The comparative scarcity of these flies in Spartanburg County where pellagra is prevalent is the reverse of the conditions of the country near the Atlantic coast where tabanids are exceedingly numerous and pellagra comparatively rare.

SIPHONAPTERA. In our studies, fleas were given particular attention on account of their known role as carriers of certain diseases and the fact that in certain localities they are very abundant and annoying pests.

It must be understood that, except where otherwise stated observations and conclusions regarding fleas refer strictly to conditions in Spartanburg County.

Somewhat to our surprise we found that, in the region studied, fleas, so far as attack on human beings is concerned, seemed to be almost of negligible importance. Reports were obtained from 154 pellagra patients or their families and of these but 10 gave positive accounts of attacks by these insects. Assuming that the reports were reliable, this may seem a remarkable condition, and allowing for a certain percentage of inaccuracy it is still practically certain that these insects are not a universal or constant pest of human beings in the locality.

While persistent attacks of fleas upon man are comparatively infrequent in Spartanburg County, they are much more common in the low sandy country lying between the Piedmont region and the coast. In the latter section the prevalence of pellagra is slight when compared with the region of which Spartanburg County is a part.

The human flea, *Pulex irritans*, is uncommon even if it exists

in Spartanburg County. We failed to find this species upon any of the numerous animals examined, nor did we succeed in collecting it from human beings.

Ctenocephalus canis and *Ctenocephalus felis* were taken on numerous dogs and cats. *Echidnophaga gallinacea*, the chicken flea, is a not uncommon pest of fowls, occurs with some frequency upon cats, dogs, and domestic rabbits, and in one instance, a report of its attack upon human beings was obtained.

In view of the fact that cats and dogs are very commonly kept, and that these animals were found to be practically always heavily infested with their respective fleas, it might be assumed that attacks upon human beings would be of common occurrence. Several reasons for doubting this assumption may be advanced. While the cat and dog fleas are less fastidious in their choice of host and more tolerant of abnormal host species than many other fleas, it is nevertheless quite certain that these species are less frequently a human pest than is usually supposed. Attacks by them upon man are not uncommon, but under ordinary conditions, even in the presence of infested animals, it by no means follows that persons associating with the animals will be infested.

It has been personally noted by one of us, in another locality, that in a house in which cats heavily infested by *Ctenocephalus felis* were kept, the fleas which were a frequent source of annoyance to the human inhabitants were all found to be *Pulex irritans*. Eggs from the flea-infested, long-haired cats must have been freely dropped about the floors, which offered excellent conditions for the development of the insects. It is equally certain that adult fleas were lost from their feline hosts, yet during a period of more than a year, every flea which annoyed the members of the household was carefully sought for and collected. They were all *Pulex irritans* and it is noteworthy that their attacks were usually made at night.

This extreme instance is cited to indicate that except at times of unusual abundance the fleas of domestic animals are not likely to attack human beings freely. It is true that individual fleas of cats and dogs ordinarily remain on human hosts but a short time, frequently leave him without biting and are probably but rarely transferred directly from man to man, factors which would tend to lessen the probability of their acting as carriers of a purely human disease.

The number of domestic animals kept by pellagrins or their families is of interest in this connection. Of 227 instances in which notes were made regarding the keeping of the smaller flea-bearing domestic animals, cats or dogs were kept in 120 cases, or 53 per cent., while none were kept in 107, or 47 per cent., of cases. This is significant in connection with the host habits of fleas which have just been discussed. If human beings in Spartanburg County

are freely and regularly attacked by fleas derived from cats or dogs, which are usually heavily infested, it seems remarkable that in so few instances were the keepers of these animals able to report their noticeable presence.

Of the 10 cases reporting attacks of fleas, dogs or cats were kept in 9 instances and none were kept by but one family. This is too small a number upon which to base conclusions. There were 149 cases in which data were secured on both the keeping of cats or dogs and the attacks of fleas. Animals were present in the houses of 78 of these cases and absent in 71. Of the former, 9 reported attacks of fleas, while, of those who kept no animals, but 1 gave such a history. The ratio of the number of reported attacks, by families in which cats or dogs were kept, to those by families with none of these animals is therefore 9 to 1 and seems to indicate that when fleas are troublesome, domestic animals are the usual source. In connection with the figures relative to the number of animals kept, it is also indicated that these animals by no means always cause the infestation of their human associates.

Sixty families who kept domestic animals and 70 who kept none, reported no attacks of fleas.

The presence of rats was reported in 38 cases, and of mice in 124. In spite of efforts to secure specimens of rat fleas, it was possible to do so in only one instance so that the degree of infestation of the rats of the region and the species occurring upon them could not be learned. The single rat secured has been determined as a cross between *Mus rattus* and *Mus alexandrinus*. The fleas with which this rat was infested proved to be *Xenopsylla cheopis*, the Indian rat flea. The occurrence of this flea at a point so far inland is interesting as is the species of its host, an animal with which it is intimately associated in the East and in many parts of its littoral range.

The facts opposed to the incrimination of fleas in pellagra transmission are: those of the sex incidence of the disease, its association with the home, the host habits of fleas, the comparative infrequency of their attacks upon human beings in the districts suffering most heavily from the disease and the inverse ratio of their abundance to the occurrence of pellagra.

In consideration of these facts it is impossible to base any satisfactory theory of transmission upon the agency of these insects.

CULICIDÆ. The abundance of mosquitoes, both of species and individuals, their agency in the transmission of important human diseases, their persistence in seeking blood and in certain instances, their close association with man cause these troublesome pests to assume a position of the highest economic importance.

Although present to a greater or less degree in most parts of Spartanburg County, they are few in number in comparison with those present in many less favored localities. The topographical

features of the district have much to do with this condition, and owing to the conformation of the land and the character of its drainage, extensive breeding areas do not exist.

When this group is considered in connection with the possibility of pellagra transmission, certain salient facts are to be noted.

The longevity with which some mosquitoes are known to be endowed, their great abundance and the predilection displayed by certain species for man's vicinity, appear to fully qualify these insects for the role of transmitters of human disease. This is amply shown to be true by the number of diseases which are transmitted by them.

Furthermore, mosquitoes are readily transported in various ways other than by their own flight to places far distant from their original habitat, with the attendant possibility of spreading infection.

Their power of flight renders the carriage of infection from house to house an easy matter, although the distance travelled is probably not great in the case of house mosquitoes and ordinarily the radius of infection conveyed by them would be correspondingly short.

It is unquestionably an argument, though not necessarily a conclusive one, against the incrimination of mosquitoes in pellagra transmission that no one species, occurring in endemic regions, has a range as wide as the geographical distribution of the disease and different species would necessarily (if the group be incriminated) assume the role of transmitters in different parts of the endemic area.

It is possible, were pellagra transmissible by mosquitoes, that several species might have the power to transmit the disease, yet there is often a high degree of specialization in insect vectors. In view of the nice physiologic adjustment between the insect host and its parasite, which is evidently necessary to the function of transmission, the foregoing assumption is not necessarily valid.

The most important fact which is opposed to the agency of these insects is the preponderance of cases among females and especially among home-keeping females. If, as indicated, the disparity is due to the greater exposure of women to infection, a cause must be sought which affects this class only and excludes those classes which show a low pellagrous incidence. In other words, the cause must be active in the day time when housewives, children, and old men are largely at home and which does not operate at night when all ages and sexes of the household are within the home influence. It is illogical to seek the cause in an insect whose activities are confined to the night hours, however well it may otherwise conform to the epidemiological and other facts of the disease.

It is to be noted, as we have said, that while mosquitoes are, comparatively speaking, not abundant in the Piedmont region

where pellagra abounds, they are a more serious pest and infinitely more numerous in the low-lying country near the coast where pellagra, though not absent, is by no means abundant.

While a very considerable number of our cases reported attacks of mosquitoes, more than an appreciable percentage of these referred to localities beyond the bounds of our territory, largely to places in the low country below the Piedmont.

The scarcity of mosquitoes was noted by all members of the party and it is highly probable that their number falls short of that required for effective disease transmission. It is admitted that diseases fail of transmission and cease to exist even in the presence of their known carriers when the number of the carriers falls below a definite point.

Certainly, it will hardly be asserted that a group of insects, represented so sparingly as are mosquitoes in this locality, can be the agent of causation of a disease having the activity displayed by pellagra in this region at the present time.

Culex quinquefasciatus and *Culex restuans* are the principal species recorded by us. *C. quinquefasciatus* was taken at a number of points and is, as might be expected, widely distributed in the county. Some water barrels were heavily infested and were producing enough mosquitoes to infest the entire immediate neighborhood. *C. restuans* is rather widely distributed and probably ranks with *C. quinquefasciatus*, as a general nuisance. *Aedes calopus*, the yellow fever mosquito was not taken within the county although quite ample facilities for its propagation exist. It is undoubtedly introduced, probably every year, but appears not to be a constant resident, the winters being usually too severe to admit of its survival. It can have no importance in the present connection in spite of its day biting proclivities and house haunting habits. Its geographical range is not as wide as the distribution of pellagra and it thrives as well in large cities as in small.

Spartanburg County bears the reputation of being almost entirely free from malaria, a reputation sustained by the small number and especially the character of the anopheline mosquitoes recorded by us. *Anopheles crucians*, a host of the estivo-autumnal parasite was encountered but once. The only other species observed was *Anopheles punctipennis* whose incrimination in malaria transmission remains somewhat doubtful. This species was met with chiefly in the vicinity of Spartanburg, a place whose physicians unanimously declare to be free from endemic malaria. Of 240 pellagra patients questioned as to the biting of mosquitoes, 160 gave positive reports while 40 only were negative.

SIMULIDÆ. Although but recently incriminated in disease transmission, the flies of the genus *Simulium* have long been known in both Europe and America as a serious pest of man and animals, their visitations assuming in certain regions the proportions of a

scourge. Much has been written regarding their blood-thirstiness and the intolerable nature of their onslaughts, the heavy loss occasioned among all kinds of domestic animals and even the death of human beings. Some of the accounts of their depredations seem to bear the stamp of a vivid imagination, but the more conservative and scientific statements, especially those of later years, are sufficient warrant for classing them among the more important and blood-thirsty of predaceous insects.

The attractive theory propounded and defended by Sambon, that these gnats are the active agents in the causation of pellagra has brought them into prominence from a new point of view.

He bases his belief in the agency of the Simuliidæ upon the following: *Simulium* affects the same topographical conditions as pellagra; in its adult state, it seems to present the same seasonal incidence; it is found only in rural districts and, as a rule, does not enter towns, villages, and houses; these flies cause severe epizootics in Europe and America. The disease, he finds, is limited to agricultural laborers (to be explained satisfactorily only by the incrimination of the gnats); the range of the group seems to cover that of pellagra, although indeed it exceeds it.⁵

Knab has pointed out that close association with man is one of the essential factors in disease transmission by insects, when, as premised by Sambon in the case of pellagra, the disease is of parasitic origin and the organism is present in the blood stream.

Simulium inhabits regions in which pellagra is endemic and in many well-watered localities presents a picture of distribution which completely covers every part of large areas. Its numbers are often great enough to cause annoyance and even injury to all warm blooded inhabitants, yet in spite of these phenomena it can not be said to show the association with man to which we have referred. The species of *Simulium* are essentially "wild" and there is no evidence, in what is known of their life history and habits, that repeated attacks on human beings with intervening periods of, at least, several days can take place with sufficient frequency to confer upon the insect the character of an effective disease transmitter. As Knab cogently insists: "It is not sufficient that occasional specimens bite man, as for example, is the case with forest mosquitoes. Although a person may be bitten by a large number of such mosquitoes, the chances that any of these mosquitoes will survive to develop the parasites in question (assuming such development to be possible) and then find opportunity to bite and infect another person are altogether too remote."⁶

Although Knab cites, as an example, the forest mosquitoes, the

⁵ L. W. Sambon, Progress Report Investigation Pellagra, Jour. Trop. Med. and Hyg., October 1, 1910. xiii, No. 19.

⁶ Frederick Knab, Unconsidered Factors in Disease Transmission by Blood-Sucking Insects, Jour. Econ. Ent., 1912, v, No. 2.

principle is of wide application and includes within its scope the species of *Simulium*, which, indeed, he excludes upon this very ground, from consideration as potential transmitters of disease.

It must be borne in mind that the essential factor here, is not the possibility that an occasional individual might sometimes be able to fulfil these conditions, but rather that the group lacks the habits (of close association with man) necessary to the establishment of the biologic relations between the vertebrate host, the invertebrate host, and the parasite of the disease.

Our observations of the group in Spartanburg County are strongly corroborative of the foregoing. We found *Simulium* breeding near or even within the limits of mill villages as well as of towns, but we failed to detect the slightest disposition on their part to seek out and attack man, to come about his dwellings, or to come in contact with him in any but the most casual and incidental manner.



FIG. 1.—Stream at edge of mill village. A breeding place of *Simulium venustum*.

The assertion that these flies cause severe epizootics is certainly not supported as regards America, at least. The heavy loss of domestic animals which occurs during severe visitations of the gnats can not be attributed to any specific disease which is com-

municated by them. All the evidence indicates that death is caused by the venom injected and by the worry and irritation occasioned by the myriad bites.⁷

Individuals are carried to or through mill villages as well as other communities, upon animals (in the ears of horses and to a less extent on cattle). This might be a limited source of supply for localities removed from the vicinity of the breeding grounds of the fly. However, it is not even known that, after a full engorgement, the female will seek a second blood meal. The extreme degree with which the flies distend themselves with blood, when undisturbed during biting, coupled with the probably short life of the adult insect, suggest that they do not ordinarily bite again.⁸

Species of *Simulium* are unquestionably found in numbers in large areas of country in which pellagra is rampant, but there is evidence to show that, contrary to Sambon's assumption, the disease is found where *Simulium* is not. We have information that pellagra occurs endemically in Barbados and as yet not only has no species of *Simulium* been found in the island, but its physical characteristics entirely preclude the existence there of the fly.⁹ There are arid regions in the United States in which the same situation exists but under different conditions and there are still other localities where these gnats are far too rare to satisfactorily account for the cases of pellagra originating in them.

That the extension of the range of *Simulium* beyond the limits of pellagrous endemicity is certainly, as Sambon says, no argument against its incrimination for there are many localities inhabited by insects with known powers of disease transmission, yet which are entirely free from the diseases which these insects may confer. In the absence of the human carrier of infection and the proper conditions, the insect vectors are innocuous.

The seasonal appearance of *Simulium*, which is supposed to correspond with that of pellagra, is probably of less significance than has been assumed. The studies of the Commission have shown that the spring-fall recrudescences of the disease do not occur, with the intensity ascribed, at least in the area under consideration,¹⁰ although the period of greatest abundance and activity of *Simulium* appears to be here, as in Italy, the early spring. Until more light is thrown upon the length of the incubation period of the disease, which seems to be variable, assumptions as to the exact time at which infection is incurred, must be received with reserve.

The disease is of essentially rural distribution but in South Carolina, it occurs in towns of considerable size. As has been

⁷ C. V. Riley, *The Southern Buffalo Gnat*, Report of Comm. Agric., United States Dept. Agric., 1886.

⁸ C. V. Riley, *ibid.*

⁹ Personal letter from Dr. H. A. Ballou, Imperial Entomologist, Barbadoes.

¹⁰ J. F. Siler and P. E. Garrison, *An Intensive Study of the Epidemiology of Pellagra*, loc. cit.

pointed out, in these places the rural element, as regards insect life, is predominant and the conditions do not necessarily preclude the occurrence of rural diseases.

In the classes of the population affected by pellagra, a very marked contrast appears to exist between European and American conditions, if European reports are accurate. The practical confinement of the disease in Italy to agricultural laborers, a class living under conditions of abject poverty, finds no economic or occupational parallel in America. Although, in Spartanburg County, the farming class furnishes a considerable percentage of all cases, the highest incidence of the disease is found among inhabitants of mill villages, whose conditions and habits of life are radically different in most essential features from those of the Italian peasant.

The fact that more than one species of *Simulium* would have to be involved to cover the entire range of pellagra is not a convincing argument against incrimination of the group but it lessens, to a certain degree, the probability of their agency. (See page 422 on mosquitoes.)

It seems to have been assumed that because the many streams of a well-watered country are infested with the larvæ of *Simulium*, the inhabitants of that country, especially those living in close proximity to streams, must be exposed to and incur the bites of the gnats.

Knowledge of the biting habits of the American species is incomplete, but it is clear that some of these species show great irregularity in their practice of seeking blood. The variation in the exercise of this habit seems to have in it a large geographic, or possibly, topographic element, for a species may be a serious pest of man in one part of its range, yet seem to ignore him entirely in another. Thus, *Simulium venustum*, one of the so-called "black flies" while proverbial for its onslaughts in the Maine woods, is only moderately troublesome in the Adirondack Mountains. In the mountains of Henderson County, North Carolina, these flies were found by one of us to be exceedingly abundant but offering no attack to man though this was courted. Sitting or standing quietly with small swarms of the flies "dancing" about the head, no attempt was made to bite. This occurred both in the presence and absence of animals which in the former case were being actively attacked. Persons of intelligence who were questioned, denied that the flies bite people and in only one instance was such a report elicited. In this case the identity of the fly was open to question, although probably a *Simulium*.

Similarly, *Simulium vittatum* is known to bite man in some parts of its habitat, but on excellent authority it is stated that in Idaho it "does not bite people."¹¹

¹¹ Personal Letter from Prof. J. M. Aldrich.

Such variation in biting habits is not without parallel among blood-sucking flies, as *Glossina palpalis* is reported by Steudel to bite man on Victoria Lake but not on Lake Tanganyika.¹²

This variability is of special significance, for it points to the fallibility of deductions based upon the mere presence of *Simulium* larvæ in a given locality without regard to the species represented and the *local* biting habits of that species.

Simulium pictipes, a widely distributed and often abundant species, does not bite man at all.

So numerous are the streams in the county that the homes of 275 pellagrins stood within an average distance of 210 yards from running water, and 215 of these streams were found to be infested with *Simulium*.



FIG. 2.—A typical breeding place of *Simulium pictipes*.

In spite of this fact, but 16 cases reported attacks of flies, the description of which could with any probability of truth, be interpreted as referring to *Simulium*. Great patience was exercised in eliciting these reports and they were carefully weighed before recording.

¹² Steudel, Deutch. Kolonialblatt, 1912, 15 Mai, xxiii, No. 10, and Beihefte zum Archiv f. Schiffs und Tropenhygiene, 1912, Mai, Beiheft 4.

The distance of *Simulium*-infested streams from the homes of 11 cases reporting bites of the fly averaged 236 yards, no data as to infestation of streams being available in 5 cases reporting bites.

The distance of *Simulium*-infested streams from the homes of 125 cases reporting no bites of the fly averaged 221 yards.

This difference in average distance is not actually great but it is interesting nevertheless. It is a striking fact that so large a number of persons living a shorter average distance, many within a few yards, from infested streams should not have been bitten and points forcibly, not only to the uncertain biting habits of *Simulium*, but to the lack of significance in the proximity of streams, even when *Simulium*-infested.

We may add that adult *Simulium* were collected in the immediate neighborhood of 46 cases who reported no bites.

The tenor of these reports is amply corroborated by those of many persons, including a considerable number who were especially well qualified through intelligence and experience with the flies in other localities or who had observed their attacks upon animals in this.

It cannot be questioned that as a pest of man in Spartanburg County, the species of *Simulium* are of small importance and that at most their attacks are delivered locally and are few in number. When comparison is made between this condition and that existing in places (including Spartanburg County) infested by stable flies, sand flies, mosquitoes, etc., the contrast is striking. These insects are always well known, even when not abundant, as we have shown in regard to mosquitoes in this locality. It is practically impossible that *Simulium* could be present and bite man in sufficient numbers and with enough persistence to satisfactorily explain the occurrence and spread of pellagra without being a well recognized and familiar pest.

Three species of the genus were encountered by us within the limits of our territory, namely: *Simulium venustum*, *S. vittatum*, and *S. pictipes*.

The former is by far the most numerous and generally distributed of the three. It was taken in its four stages, adults being collected about twelve times, either in the act of attacking animals or of ovipositing.

Simulium vittatum was taken in the larval, pupal, and adult stages, and also probably in the egg. Adults were twice collected while attacking horses or mules.

Simulium pictipes occurs quite locally in large colonies where suitable conditions exist. These consist of a rapid flow of clear water over boulders and sheets of rock in the larger streams. Such conditions are not very frequently met with in this vicinity owing to the turbidity of most of the creeks and rivers of the locality.

There are no records of this species attacking man and it need not be considered in the present connection.

The facts as set forth above do not support the incrimination of *Simulium* in the transmission of pellagra.

HOUSE AND BLOW FLIES. So abundant is the current literature regarding the nature, habits, and pernicious activity of the house fly, that a general discussion of this well known and troublesome species seems superfluous. Its familiar role as an active mechanical carrier of bacterial disease, however, renders it of the highest economic importance and necessitates its consideration in the present study. The possibility of the transmission of pellagra by house flies through the contamination of food to which they have access, or by direct mechanical transmission of the virus (if it exists) from man to man, is evident.

Musca domestica was present everywhere and was usually extremely numerous. Sanitary conditions were only too frequently such as to attract, if not actually to breed, the filth-loving species of flies, but in the more or less congested village and town communities there was no strict correlation between the sanitary condition of the individual premises and the number of flies present. Even well-kept homes offered sufficient attraction to insure their infestation by the flies which in every neighborhood were present in large numbers.

In mill villages the principal source of house flies appeared to be the accumulations of manure of horses and cattle at the stables and sheds in which the draught animals of the mill companies and the cows of the operatives were sheltered. In those villages in which milch cows are allowed to be pastured and stabled indiscriminately through the village, breeding occurred almost everywhere in the haunts of the animals.

The type and condition of privies in mill villages are conducive to the presence and breeding of this species as well as to the carrion flies, *Calliphora*, *Lucilia*, and the *Sarcophagidæ*. Upon otherwise cleanly premises, the privy was often a source from which flies emanated and was a standing menace of infection.

Musca domestica was found in and about the homes of practically all of the cases studied as well as those of non-pellagrins. In a very few instances case histories make no mention of the species, but this is unquestionably due to inadvertence.

Until the transmissibility of pellagra is disproved or the nature of its virus and the manner of its communication are known, the house fly must be regarded with suspicion.

STOMOXYS CALCITRANS LINN. The biting stable fly is an insect of cosmopolitan distribution and great economic importance. In most localities within its habitat it is very abundant, and though it feeds by preference upon domestic animals, man is very frequently attacked. Attacks upon human beings are more common when the

animals upon which it normally feeds are not available and its onslaughts are often severe and persistent.

The injury inflicted upon live stock is often very serious and many deaths are caused during the occasional outbreaks of this fly, which sometimes occur under unusual conditions favoring its inordinate propagation. At all times it is a serious pest of animals and has been incriminated in the transmission of trypanosomal diseases of animals, anthrax in animals and man, and of anterior poliomyelitis in man.

While *Stomoxys* is, as a rule, more abundant in country districts, owing to the greater facilities for propagation which it finds in the rural environment, it is usually common in towns and cities of even the largest size. In the very heart of the great cities and in such neighborhoods as practically preclude the possibility of its breeding, it may be seen in considerable numbers along the main thoroughfares. The vicinity of markets and wharves is especially likely to be heavily infested and this is the case even when scrupulous scavenger work renders its propagation at the spot impossible. The source of supply under such circumstances may be far removed and the fly population maintained by the constant arrival of individuals which accompany animals on their journeyings or which are guided by their sense of smell in independent flights from more or less distant localities.

The stable fly will breed in unmixed manure of horses and cattle, in such materials mingled with particles of straw and in rotting straw alone. While we have repeatedly bred the stable fly in large numbers from naturally infested, unmixed dung of horses and even a few individuals from that of cattle, the observations of Bishopp during a recent severe outbreak of the fly in north Texas, indicate that decaying straw is the material most favorable to its propagation. His careful work shows conclusively that in the order of preference, the substances in which *Stomoxys* will breed are oat, rice, barley, and wheat straw, horse manure, lot manure, and cow manure; that pure horse and cow manure are less attractive to the fly than when mixed with a considerable quantity of straw and that under a combination of conditions of plentiful moisture and abundance of rotting straw, breeding will occur at its maximum intensity.¹³

Similar observations have been made by Lucien Ichès in Argentina.¹⁴

There is a direct relation between the presence and numbers of domestic animals and the abundance and distribution of this fly, which wanders far from its breeding places in search of food and will follow animals for long distances. This, however, is not its

¹³ F. C. Bishopp, The Stable-Fly (*Stomoxys calcitrans* L.). Jour. Econ. Ent., 1913, vi, No. 1.

¹⁴ Lucien Ichès, *Stomoxys calcitrans* L. et le bétail Argentin., Bull. Soc. nation Acclimat., France Ann., 1909.

only means of dispersion, as steamships, passenger trains, and those carrying live stock upon railroads are a common aid to its migration. We have encountered the species under all these conditions and have seen it carried for hours on the under side of an automobile top, in spite of wind and jolting over rough roads. In the latter case, the fly appeared to be full fed and, resting in this way after engorgement, it would be more likely to remain in such a situation and to be carried to a new locality. This is of special significance in connection with disease transmission. It is evident that flies carried in the ways mentioned, if infected or acquiring infection en route would have the power to carry the disease to a new locality remote from endemic foci. Particularly would this be the case if opportunity for feeding during the journey was lacking, as the hungry fly would upon arrival immediately seek a meal of blood, human or animal, and thus transmit the infection. An instance of the persistence of *Stomoxys calcitrans* in seeking blood was observed by us on the coast of South Carolina. The six occupants of a fishing boat were attacked, more than a mile from land, by numerous flies which suddenly appeared and which had evidently not been carried in the boat. It must be borne in mind that the stable fly is not attracted to offensive substances, and the odors from the fish-scented boat can hardly have played a part in drawing the flies so far from land. All the persons in the boat were bitten one or more times and the bare-legged boatmen greatly annoyed. They stated that such an occurrence was very common and that they were frequently attacked when at sea. *Stomoxys calcitrans* is very abundant along this line of seacoast and in the adjacent country. The day was clear and hot with a gentle off-shore breeze.

Although primarily a pest of live-stock, infesting and breeding in situations frequented by domestic animals, this fly often invades dwellings. While indoors it attacks the human inhabitants and we have even seen it more numerous in living rooms of mill dwellings than the ever-present house fly. It must be understood that in such cases the latter species was somewhat less numerous than usual.

Stomoxys has the habit of utilizing several hosts in order to secure a single meal, either from choice or because when dislodged by one host it flies to another.¹⁵ This habit is important in connection with disease transmission. Especially is this the case in the interior of dwellings where all the members of the household would be exposed to the infection, if transmissible, which might be carried by one of its members.

It is, moreover, within the possibilities that a puncture of the

¹⁵ C. T. Brues and P. A. E. Sheppard, The Possible Etiological Relation of Certain Biting Insects to the Spread of Infantile Paralysis, Jour. Econ. Ent., 1912, v, No. 4; Herbert Osborn, Insects Affecting Domestic Animals, Bull. 5, N. S. Bu. Ent. United States Dept. Agric., 1896; H. Maxwell-Lefroy, Biting Flies of India, 1907.

skin by an infected fly's proboscis might introduce the infection although no blood is drawn. This has been shown to be experimentally possible in the non-mechanical transmission of trypanosomiasis by *Glossina palpalis*.¹⁶

As has been pointed out, the members of the household who suffer most from pellagra are those who pass the most time in the home or its vicinity in the day time and it is these members, the females, who are most exposed during daylight hours to the attacks of *Siomoxys*.

As we have stated, *Stomoxys calcitrans* is not attracted by the odors of putrefaction. Hog-pens and privies are not inviting to it, nor is it apparently drawn to the nasal secretions of animals nor presumably to those of man as is the house fly, this discrimination being of importance in connection with the carriage of certain diseases.

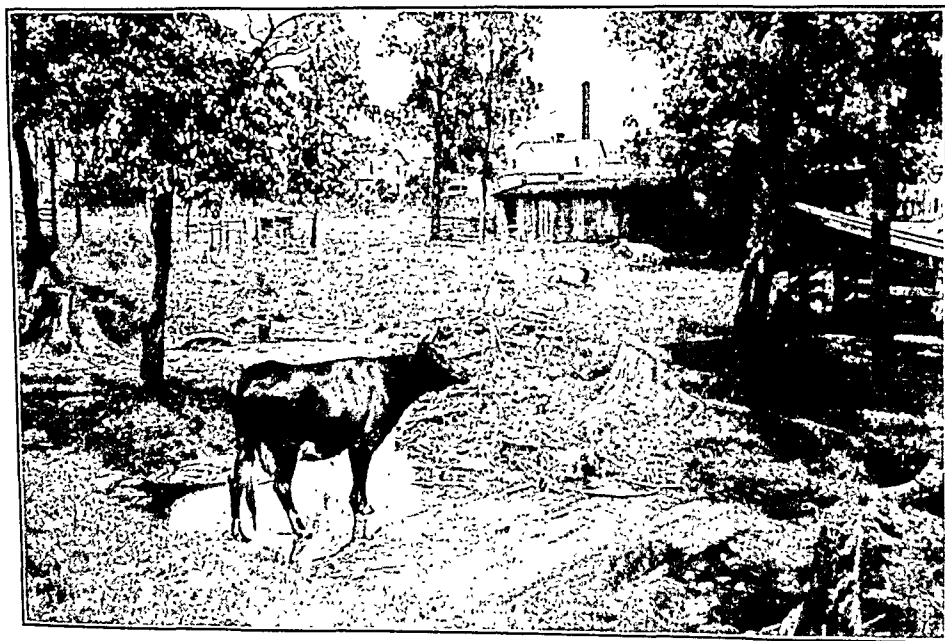


FIG. 3.—A pasture provided by mill authorities for cows, etc. of operatives. Note cow-sheds hog-pens, and proximity of dwellings. The stream in foreground breeds *Simulium*

The stable fly is exceedingly abundant and generally distributed in Spartanburg County. In most of its geographical range the species is of importance in its relation to live stock and, our studies indicate, that it is also a pest of man with which it is necessary to reckon. No part of the region is free from this fly and it may be seen in numbers upon the streets of towns and villages, about barnyards, modest dwellings, and pretentious residences. Every

¹⁶ A. D. Fraser and H. L. Duke, Proc. Roy. Soc., August 24, 1912, Ser. B, lxxxv, No. B, 581; Abs. Sleep. Sick. Bull, 1912, 4, No. 40.

team upon the roads is followed, and every cow in pasture or barnyard is constantly exposed to its attack during the daylight hours.

As a part of the study devoted to this species, statements regarding its biting were obtained from as many persons as it was possible to interview, the questions being put to pellagrins and their families as well as to non-pellagrins. In obtaining reports on the biting habits of the fly, great care was exercised not only to be sure of the identity of the fly of which the individual was speaking, but to suggest nothing which might influence the tenor of the report. All reports were rejected which after careful consideration seemed doubtful, either as to the identity of the insect or the details of the statement.

Reports relative to the biting of *Stomoxys* were obtained from 227 pellagra patients and of these 115, or 50.7 per cent., gave positive histories of attacks and to these should be added 10 from members of families of pellagrins who could not themselves recall having been bitten. In 112 cases, or 49.3 per cent., the patient could remember no bites or was positive that none had been inflicted.

In addition to the above reports, many persons not included among our pellagra sufferers recounted experiences with the persistence of attack and voracity of the fly.

Close attention was given to the presence of the fly in such situations as would facilitate its attack upon the inmates of dwellings of all descriptions, that is, its presence or absence about the yards and premises, especially upon the outside of houses near open, unscreened windows, upon porches, and the interiors of dwellings. The distribution of the fly in the latter situation has some significance, and observations were made to determine its preference for different kinds of rooms.

Stomoxys was present about premises, yards, sides of house, or porch of the homes of 136 pellagrins, being abundant in 94 instances.

An illustration of the universal distribution of the fly was seen in a mill village which was studied with special care. This village contained 113 inhabited buildings, including the company's store and office. Stable flies were found about 103 of these buildings and inside of several of them. It was found that the distribution varied somewhat, houses seemingly free from the flies at the time of our first visit would be infested at a later time, the reverse also being true. Nevertheless, there were few dwellings about which individuals could not be found at any time and it is to be assumed that they were present at all buildings more or less frequently.

For various reasons, it was quite often impossible to make a careful search of the interiors of pellagrous dwellings and conditions of weather, light, etc., were sometimes unfavorable to the presence of the flies at the time of inspection and made their discovery

difficult. Enough observations of its presence were made to show that invasion of human habitations is of common if not regular occurrence.

Its presence was noted in more than 30 dwellings of pellagrins, in fully half of which it was abundant, and in one instance a partial count showed 30 individuals.

The character of the rooms frequented by the fly has a bearing, not only upon the opportunity for attack, but upon its general habits. Strong preference was shown for the living rooms and in more than half of the houses studied these were the only rooms infested. In about one-fourth, flies were found in both living rooms and kitchen, while in only one instance was the kitchen alone infested and then by only one or two flies. In the houses of mill workers the living room is usually also a bed room. It will be seen that in case of illness or during moments of relaxation, the occupant of a bed in a *Stomoxys*-infested room invites the attack of the fly. It was evident that in addition to the odors of putrefaction, those of cooking are not attractive to this species, which is in strong contrast to habits of the house fly. The difference in domestic habitat of the two species is very striking, kitchens frequently swarming with house flies where living rooms were only moderately infested, the same houses showing infestation of *Stomoxys* in living rooms only.

MANGEMENT OF LIVE-STOCK IN MILL VILLAGES, ETC. The relation of domestic animals, especially horses and cattle to the presence and abundance of *Stomoxys* is so important, that a knowledge of the number and management of these animals is essential to a study of the bionomics and distribution of house and stable flies.

Cattle, horses, mules, and hogs are very commonly kept in Spartanburg County especially upon farms, while in the cities, towns, and hamlets, many of the non-farming residents maintain milch cows and driving or draft animals. The inhabitants of the mill villages, also keep many cows, one cow to about three families being a fair average.

Upon farms, the stables and sheds in which animals are housed are usually placed about the barnyard at no great distance from the dwelling. Manure is often allowed to accumulate, and the floors of the outbuildings are frequently covered by a deep layer of droppings, the fresher portions heavily infested with fly larvæ. These conditions are by no means invariable and in many instances manure is not allowed to accumulate about the stable or barnyard, but is disposed of more or less promptly.

The definite allotment of land for purposes of pasturage is not invariable and, especially when but a few head of stock are maintained, they are pastured in a more or less indiscriminate fashion upon waste land, in lanes, woods, and such situations as prevent danger to growing crops. As a rule the milch cows are brought

to the barn to be milked, and draught-stock is invariably stabled and fed. Hogs are sometimes pastured but are frequently confined to small yards or pens which, too often, are unsanitary in the extreme and highly attractive to house and blow flies.

In cities and small towns, with the exception of the poorer dwellings, many, if not most, residences are provided with a stable in which a horse or cow, sometimes both, are sheltered. Depending somewhat upon density of population, these animals may be pastured upon vacant lots, road sides, and door yards or they may be confined to small yards adjacent to the stable. The care given the animals and their quarters varies greatly, but ample opportunity for fly propagation occurs. Hogs are usually excluded from the corporate limits of the larger communities.

In most of the mill villages there are no regulations regarding the keeping of domestic animals, including hogs. Cows are pastured indiscriminately about streets and village lots. They are stabled in small shacks upon the house lots of their owners or even under the houses when these stand upon sloping ground and sufficient room for this purpose is afforded. The cows are milked and fed grain, etc., on the premises, and their droppings are a source, sometimes a prolific one, of fly breeding.

In a few of the mill villages a common pasture is provided in which the cows of the mill operatives must be kept. They are not permitted upon the streets or house lots, and rough shed stables are usually provided in which the animals are fed, milked, and sheltered in inclement weather. These sheds are roughly constructed and although the droppings are removed from the stalls at intervals, piles of manure are left for varying periods in the immediate vicinity providing breeding places for great numbers of flies.

The plan of exclusion is an excellent one, but, unfortunately, the benefit is minimized by certain details of its application. Pastures are usually contiguous to the village, the nearest houses often standing within 100 feet of the pasture boundary and cow sheds. In one instance the pasture is almost at the centre of the village and is closely approached on three sides by the dwellings. In another village there are two pastures at opposite sides of the village and a large part of the community is thus exposed to the flies frequenting or produced within them. The rule of exclusion is not always rigorously enforced and exceptions are sometimes permitted; calves are occasionally, either openly or surrepticiously, kept about the owner's house and in one instance which came under our notice a cow was regularly brought for milking to the owner's house in spite of the regulation and an examination of the surroundings showed a large number of stable flies about the house adjoining that of her owner, whose premises were comparatively free from them.

A fact bearing upon the importance of domestic animals in connection with *Stomoxys* in its relation to human beings is that of

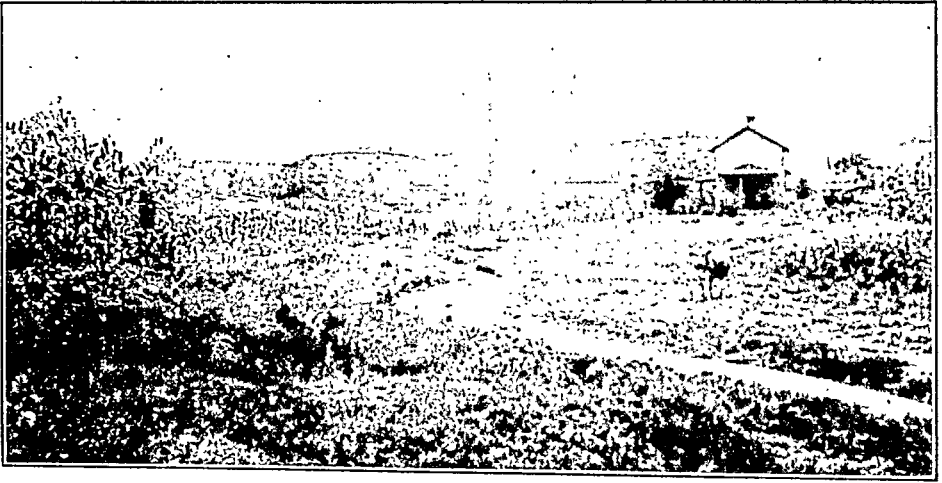


FIG. 4.—Open commons used as cow pasture by mill operatives. The stream in foreground is an active *Simulium* breeding place. Houses of operatives in middle distance.



FIG. 5.—Part of a mill pasture with hog-pens and dwellings. Nearest house is about sixty yards from fence.

attack upon milkers. Although in the presence of animals which the fly normally prefers to man, the comparative quiescence of the persons so engaged, renders them peculiarly liable to attack, while those attending to and associating with cattle while actively engaged upon their duties may escape. That the milker is frequently attacked is shown by the reports we received.

But 21 pellagrins of our series had been in the habit of milking cows, and 2 of these were not questioned regarding the fly in this connection. Of the remaining 19, 14 or about 74 per cent., stated that they had been bitten while milking, and a considerable number of non-pellagrins made similar statements.

The comparative distribution of *Stomoxys* in urban, rural, and mill districts is interesting. Infestation of premises—the presence of *Stomoxys* upon the outside of houses, upon porches and in the immediate vicinity—in places from which entrance to the house or attack upon its inmates would be easy, occurred most frequently in mill villages. In these villages 97 per cent. of the homes visited were infested in the way described while of rural and farm homes 67 per cent., and of urban, 50 per cent. were similarly frequented.

The explanation of this seems to be that in the presence of domestic animals, the stable flies in the immediate vicinity will be concentrated upon and about them and many follow them when driven to work or to pasture, so that in the absence of the animals the infestation of the premises may be greatly lessened or the flies be so few as to escape notice. In the mill villages, the flies, separated from passing teams or cattle become generally distributed, seeking shelter and food among the dwellings, and it is significant of the truth of this explanation that in mill villages whose rules do not exclude cows from the village precincts, the number of stable flies present about the houses is more variable although apparently larger in the aggregate than in those villages which practice exclusion.

In comparing the reports of biting by *Stomoxys* received from pellagrins of the three classes, it is interesting to note that 55 per cent. of the reports received from mill cases were positive; 54 per cent. from rural cases were also positive; while but 13.4 per cent. of the urban cases could recall attacks by the fly.

It will be seen that the highest percentage of reports of bites by *Stomoxys* was received from the mill villages which also furnish the greatest number of pellagra cases. The rural districts follow closely in their percentage of positive reports though there is a greater discrepancy between pellagra incidence in the mill villages and that of these districts than is indicated in the reports. This fact might be accounted for by the lack of congestion of population in the rural sections with a lower percentage of possibly infected flies.

These reports evidently indicate that there is a definite correlation

between the abundance of *Stomoxys*, the character of its distribution and its biting of man.¹⁷

SUMMARY. Our investigation was entered upon with no bias in favor of the infectiousness of pellagra or its transmissibility by insects. In the nature of the case, however, and as a basis for our work, it was necessary to assume that both were among the possibilities.

No preconceptions as to the involvement of any particular insect were indulged, and our conclusions regarding individual species of insects are based upon the epidemiological picture of pellagra, mainly as presented in Spartanburg County, and upon the habits and distribution of the insects as observed by us and as elsewhere recorded.

Ticks, lice, bed bugs, cock roaches, horse flies, fleas, mosquitoes, buffalo gnats (*Simulium*), house flies, and stable flies (*Stomoxys*) were under consideration. Of these, horse flies have nothing and cock roaches little to support them.

Ticks and fleas are excluded on account of their scarcity and the nature of their biting habits. In view of these characteristics, it is doubtful if even the existence of an animal reservoir of infection would bring the groups into prominence.

Lice and bed bugs do not account for the sex or age incidence or the rural nature of the disease; the scarcity of the former is an additional reason for its exclusion.

The rarity of mosquitoes here and the lack of coincidence between their distribution and that of pellagra for the State in general, together with the night-biting habits of the local species, which fail to account for the sex incidence, seem sufficient cause for their elimination.

House flies (*Musca domestica*) should be active if the malady is an intestinal infection in which the germ is passed with the feces, with contaminated food acting as the vehicle of infection.

The buffalo gnats (*Simulium*) should be eliminated, principally by the facts of their biting habits and lack of those of intimate association with man, also possibly by their comparatively moderate abundance (in our territory). We find that in Spartanburg County they are hardly known as a pest of man and when they do attack him, it is very locally and largely confined to field workers. Had Sambon's theory not been advanced, these flies could hardly have attracted suspicion of any connection with pellagra in this country.

The stable fly (*Stomoxys calcitrans*) displays certain salient characteristics which seem to qualify it for the role of a transmitter of pellagra.

The range of this one species covers and exceeds that of pellagra;

¹⁷ Allan H. Jennings and W. V. King, One of the Possible Factors in the Causation of Pellagra. Jour. Amer. Med. Assoc., January 25, 1913, lx.

its seasonal activity, likewise, is coincident with that of the disease and, although its period of greatest abundance is somewhat later than the maximum intensity of pellagra, its appearance in spring precedes that of most of the spring recurrences and new cases, at which time it is already abundant; it is an abundant species, its abundance being most manifest in rural districts thus corresponding with the rural nature of pellagra, its numbers amply fulfilling our conception of those necessary to effective disease transmission; it bites by day only, thereby offering an explanation of the phenomenon of sex incidence and the related one of age distribution; it is intimately associated with man and habitually infests his vicinity and enters his dwellings; it bites man frequently and persistently; its longevity seems sufficient for the development of a hypothetical causative organism; it is readily and frequently carried long distances and might thus account for the occurrence of sporadic cases of the disease.

REVIEWS

SURGERY OF THE EYE, A HAND-BOOK FOR STUDENTS AND PRACTITIONERS. By ERVIN TÖRÖK, M.D., Surgeon to the New York Ophthalmic and Aural Institute; Ophthalmic Surgeon to Beth Israel Hospital; Consulting Ophthalmologist to the Tarrytown Hospital, and GERALD H. GROUT, M.D., Assistant Surgeon to the New York Ophthalmic and Aural Institute; Instructor in the Eye Department, Vanderbilt Clinic; Consulting Ophthalmologist to the Bellevue Hospital, First Division. Pp. 509; 509 illustrations, 101 in colors, and 2 colored plates. Philadelphia and New York: Lea & Febiger, 1913.

THE purpose of this work is primarily to give to the student a clear and detailed description of the steps of the operations necessary in the surgical treatment of diseases of the eye; in this the authors have succeeded admirably. Indeed, it is difficult to see how the descriptions could be improved upon. But the book is more than this. It sets forth briefly and clearly the surgical anatomy of the eyeball as a whole, and of the accessory structures before entering into a description of the individual operations. The different pathological conditions requiring operative interference are also clearly described and where there are several procedures for attaining the same end, the proper selection is indicated. Every step almost is illustrated by a diagram; inspection of the latter alone gives a fair conception of what is intended to be conveyed; the illustrations are of inestimable value to the descriptions.

The first chapter is devoted to considerations upon eye operations in general, such as the preparation of the patient, the operating room, illumination, preparation of instruments and dressings, anesthesia, postoperative treatment, and complications. A second chapter deals with the instruments, most of those employed being figured, many in their natural size; a list of the same covering two pages completes the chapter (armamentarium).

The surgical anatomy of the eyeball is exceedingly well described in the brief space of a short chapter.

As evidence that no operative procedure is considered too insignificant, we find minute directions for the removal of foreign bodies from the cornea, whether upon its surface or in the deep layers; the procedure to be followed in the case of foreign bodies which have partially penetrated into the anterior chamber (keratome passed into the anterior chamber behind the foreign body)

is of course described. The localization and treatment of a foreign body within the eyeball and orbit is very properly compressed into a small space, as this part of ophthalmic surgery is quite a specialty in itself and requires special apparatus and training.

When considering operations upon the ocular muscles, whether resection or advancement, the authors appear to favor the former based upon "pathological examination of eyes after advancement which has shown that the advanced muscle becomes adherent to the sclera at its new insertion and the space intervening between this point and its old attachment. So it would seem that the advancing of the insertion of the muscle *per se* was of no value and the improvement obtained by the operation was due to a shortening of the muscle the same as in resection. The point of leverage in both cases is the original insertion of the muscle."

The writers make no comparison between the advantages of tenotomy and its opposite, which they entitle operations to strengthen the action of an ocular muscle, as against the former which is intended to weaken the same. Both types of operation are declared to be imperfect, as the final amount of weakening or strengthening can never be foretold in either case, this being particularly true of tenotomy. Operations in heterophoria are said to be indicated only in high degrees, when other measures fail to give relief. We readily draw the inference that the authors are no advocates of partial graduated tenotomies in heterophoria. We find no reference to orthoptic training in strabismus and this perhaps quite properly, as the latter is not a surgical procedure.

In the treatment of diseases of the lacrimal passages, Toti's operation is well spoken of upon the basis of satisfactory personal results. Probing, styles, and stricturotomy are not recommended. The indications for extirpation of the sac are given, but comparison with Toti's operation is not made. Lagrange and Elliott's operation are described in the treatment of glaucoma, as is also Heine's method of cyclodialysis. The theory of the latter seems to be faulty upon the basis of anatomical examinations which showed that the ciliary body had become firmly reattached to the overlying sclera.

To the operations for cataract as is natural, is given the most space. The descriptions are excellent and leave little to be desired. We have not found any reference to Smith's Indian operation, with the exception of eight words in the description of the anatomy of the lens, where it is stated that the capsule is left behind in the operation for cataract "unless the lens is extracted in the capsule."

Dr. Arnold Knapp in the short introduction to this work makes the statement "that the authors have succeeded admirably in their project." The reviewer heartily endorses this opinion.

The publishers' work is well done. The type, paper, and press-work leave nothing to be desired.

T. B. S.

CYCLOPEDIA OF AMERICAN MEDICAL BIOGRAPHY. By HOWARD A. KELLY, M. D., Professor of Gynecologic Surgery at Johns Hopkins University, Baltimore. Vol. I: Pp. 509; 10 portraits; Vol. II: Pp. 545; 24 portraits. Philadelphia and London: W. B. Saunders Company, 1912.

No more servicable addition to the literature of American medicine has been made in recent years than Dr. Howard A. Kelly's monumental work on American medical biography from 1610 to 1910. The labor involved in compiling the two volumes which comprise this work has been enormous, and we indeed owe a debt of gratitude to the man whose energy and enthusiasm prompted him to undertake such a stupendous task. As a result of his zeal we possess what has been much needed, an up-to-date and complete, yet convenient biographical cyclopedia.

The greater part of the two volumes consists of a series of short biographical sketches alphabetically arranged. These sketches give a brief outline of the lives of twelve hundred distinguished medical men who have lived and labored in the United States and Canada during the past three hundred years. The completeness of the list is surprising, and omissions, if there are any, must be few, for the names given include all who have been conspicuous as investigators, writers, teachers, and leaders in medicine and the various medical sciences on this continent. For one man to write such an array of biographical notes would have been well nigh impossible. Dr. Kelly therefore, wisely associated with himself a group of collaborators who were particularly interested in work of this kind. Their names are mentioned in the preface and their initials appear after the sketches that each has written. The result of this method is a collection of biographies that are bright, interesting, and sufficiently varied in style to prevent the monotony which is too apt to pervade books of this type.

The most interesting part of the work is a series of nine able introductory articles describing the development and progress of the various medical specialties in America, namely: Anatomy, surgery, gynecology, obstetrics, ophthalmology, laryngology, medical jurisprudence, army and navy, and women in medicine. These articles take on an added value and authority from the fact that they have each been contributed by a separate author who in every instance is well qualified to perform the task. Happily the subjects of gynecology and obstetrics have been written by Dr. Kelly himself.

The numerous portraits of particularly well known and distinguished medical men that appear throughout the book, add considerably to the beauty and interest of the work.

The enthusiasm with which the work will undoubtedly be received throughout the country should assure Dr. Kelly that his

years of painstaking effort in the preparation of this book have met with the full appreciation of his colleagues and of all who take pride in the long list of tireless and hardy workers whose names will ever be associated with the advances and triumphs of American medicine.

G. M. P.

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M. D., Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital, etc. Assisted by LEIGHTON F. APPLEMAN, M. D., Instructor in Therapeutics, Jefferson Medical College, Philadelphia, etc. Vol. II, June, 1913; pp. 449; 131 illustrations. Philadelphia and New York: Lea and Febiger, 1913.

MANY interesting volumes of *Progressive Medicine* have been reviewed in these columns, but none has furnished more instructive and important information than is to be found in Volume II for this year, which has been recently published. The opening contribution of 67 pages by William B. Coley deals exclusively with hernias, the many and varied phases of which are carefully discussed. John C. A. Gerster follows this with an admirable article of 118 pages on recent advances in surgery of the abdomen, exclusive of hernia. Under the stomach he dwells at length upon recent important observations on the Röntgen ray diagnosis of various gastric conditions and upon gastric ulcer. The small intestine, appendix, and large intestine are next discussed. Under the latter his views on the surgical treatment of constipation, with special reference to the notable work of W. B. Cannon and Arthur Keith on the anatomy and physiology of the large bowel, and Coffey's work on gastro-intestinal stasis and ptosis are well worth careful study by both internist and surgeon. Under the head of the liver, bile passages, and portal vein Gerster not only deals with a number of surgical considerations, but also invades the realm of medicine to the extent of devoting four pages to Roger's emetine treatment of amebic disease.

John G. Clark furnishes his always interesting review of gynecology. Very properly a little over one-quarter of his 116-page contribution is devoted to the cancer problem. Almost as much space is given to a discussion of Röntgen therapy in gynecology, especially in reference to uterine myomas. Uterine malpositions, menstruation, the ovary, gonorrhea in the female, tuberculosis of the kidney, cystitis and urethroscopy, and sterility in women may be mentioned specifically from among the many other important subjects upon which he lays stress.

The medical section of the volume consists of Alfred Stengel's 120-page article in which the various elements of the blood, including the bone marrow are first discussed. Pernicious anemia is disposed of in a few pages, whereas 18 pages are devoted to leukemia, indicating the trend of investigation during the past year. Primary splenomegaly and polycythemia are also dealt with at some length, as is hemorrhagic disease. After a brief survey of the adrenal glands and their diseases, Stengel devotes about six pages to gout and then enters upon a careful consideration of recent work on diabetes. Somewhat over a fourth of his entire contribution is given over to a discussion of the thyroid gland, various conditions affecting it, and exophthalmic goitre in particular.

In a short review of some 30 pages on ophthalmology, Edward Jackson contributes the concluding section. Under the various anatomical divisions of the eye he takes up the contributions of importance that have appeared during the past year in this particular field of work.

G. M. P.

THE CATARRHAL AND SUPPURATIVE DISEASES OF THE ACCESSORY SINUSES OF THE NOSE. By ROSS HALL SKILLERN, M.D., Professor of Laryngology, Medico-Chirurgical College, Philadelphia. Pp. 389; 247 drawings and 5 colored plates. Philadelphia: J. B. Lippincott Company, 1913.

As he states in his preface to this able work, the author has endeavored to present in the English language a comprehensive and complete text-book on the nasal accessory sinuses. Heretofore the student of the many problems inspired by the vast interest in this subject that has arisen in recent years, mainly through the researches of the German school, has been compelled to seek for information in the works of Hajek, Zarnico, and others in German, or Luc in French. The only work in English dealing extensively with nasal sinusitis has been that of Logan Turner, of England.

The present volume bears ample evidence of the great amount of work and painstaking care of the author as shown by the references, well arranged at the foot of each page, there being no less than 586 of these, comprising an almost complete bibliography of the subject.

The work is systematically arranged for convenience in study and reference, starting with a chapter on general considerations, which includes anatomy, physiology, differential diagnosis, and treatment. The four succeeding chapters deal with the respective sinuses in detail, namely, the maxillary sinus, the frontal sinus, the ethmoid labyrinth, and the sphenoid sinus. The plan in each of these is to give the detailed surgical anatomy, etiology, diagnosis, symptoms,

technique of the different procedures necessary for diagnosis and treatment and lastly the surgery, intra- and extra-nasal.

Of the many unique and admirable features of the book one can only mention a few, but the first point that impresses the reader is the number and quality of the illustrations by such well-known artists as the Fabers. Almost all of these are original, being made from the author's own anatomical preparations and are drawn strictly to illustrate the text. As an instance of this, no less than seven large drawings from photographs depict every step of Dahmer's operation on the maxillary sinus with such clarity that a novice must understand; six show the preturbinal method; six the Caldwell-Luc; while ten are required to amplify the description of the Killian operation on the frontal sinus. These are merely the most striking instances of a feature that adds greatly to the merit of the work. But by no means are all the illustrations of operative procedures; many excellent anatomical and pathological drawings being included.

It is well known to any student of the sinuses that more variations exist in the bony structure and arrangement of these cavities than in any other part of the body and it is this that lends interest to the study, as well as difficulty and uncertainty in treating their diseased conditions.

Many of these anomalies are shown, taken from specimens of the author and others, and every endeavor is made in the text to guard the operator from being misled. The descriptions are systematic and clear and every phase of the subject is covered; so thoroughly in fact that it is distinctly a text-book for the specialist rather than for the general practitioner.

As the first American work on the subject it should appeal to all those practising the specialty of rhinology and should be almost equally valuable to the ophthalmologist, and is not out of place in the library of the up-to-date internist.

G. M. C.

INSOMNIA: ITS CAUSES AND TREATMENT. By SIR JAMES SAWYER, of London, Doctor of Medicine of the University, Fellow of the Royal College of Physicians. Second edition; pp. 107. Birmingham: Cornish Brothers, 1912.

THIS small book consists of the first three chapters of the author's "Contributions to Practical Medicine," fifth edition, 1912, and is published separately for the convenience of the profession.

This volume makes delightful reading. In the first chapter the causes of insomnia are discussed and the usual theories given. The second and third chapters are the important ones. In them treatment is discussed by drugs, exercises, general methods, psychic treatment,

etc. Besides there is a useful summary at the end. In a word, this small volume is full of good practical suggestions based upon sound logic and experience. It is delightfully written and contains references to the foibles of some of our celebrities. Accordingly, to induce sleep beer was used by Lord Bacon, while King George III slept with his head on a hop pillow, and even King Edward VII was addicted to this. Charles Dickens' plan was to stand at his bedside until he felt chilly, and then hop into bed and go to sleep, and the illustrious William Harvey was in the habit when he was "hott-headed" and his thoughts stirring to such an extent that they would keep him from sleeping, of arising out of bed and walking out of his chamber in his shirt until he began to shiver, and then would return to his bed and sleep comfortably. T. H. W.

THE COLLECTED WORKS OF CHRISTIAN FENGER, M.D., By LUDVIG HEKTOEN, M.D., Professor of Pathology at Rush Medical College. Two volumes; averaging 525 pages each, illustrated. Philadelphia and London: W. B. Saunders Company.

AMERICAN surgery owes much to Christian Fenger. His work in applying the knowledge of pathology and pathological anatomy to the furtherance of surgery was pioneer in this country. He also was one of the first to embrace the principles of Lister and to point out the great advantage in results to be obtained by those methods. These volumes represent the praiseworthy effort to preserve in memorial form the collected writings through the medium of which so great an impress was made upon his contemporaries. The breadth of his interest may be seen by a cursory perusal of the titles of the 75 papers which embrace almost every branch of surgical practice.

Many of the contributions may be recommended as models of scientific writing in that the conclusions are based upon an orderly array of evidence carefully gathered, thoroughly digested, and simply presented. The collection is of historical value and of special interest to those whose fortune it was to have been associated in any way with the gifted and stimulating author. D. B. P.

DISEASES OF THE EYE. A MANUAL FOR STUDENTS AND PRACTITIONERS. By J. HERBERT PARSONS, D.Sc., M.B., B.S., F.R.C.S. Second edition. Pp. 684; 328 illustrations. Philadelphia: P. Blakiston's Son & Co., 1912.

IN the second edition of Parson's *Diseases of the Eye* the author has revised the text, adding several new sections, and has intro-

duced additional illustrations and colored plates. The book is one of the best of the moderate-sized manuals on diseases of the eye, and is readable because of its simplicity and directness of style. Especially to be recommended as of value to the student are the sections on physiology and elementary physiological optics. There are 17 full-page plates, all but two of which are colored. The productions of fundus conditions are notably good, much better than those in many more pretentious text-books, especially in those published in America. Despite the fact that Mr. Parsons' writing has been largely in the domain of ocular pathology, this portion of the subject has not been allowed to overshadow the others, and the clinical descriptions are good. Treatment, especially from a constitutional viewpoint, is perhaps too briefly considered, but those who wish to pursue the subject more deeply are referred to Fuchs' text-book, and for treatment to Hanke's *Treatment of Diseases of the Eye*, which was translated by Coats and the author. Three appendices are given; one containing a method for preliminary investigation of the patient, the second therapeutic notes, and the third, the requirements for admission into the public services. On the inside of the back cover is a set of Holmgren's wools for color blindness. It is pleasure to cordially recommend the volume.

E. A. S.

THE TECHNIQUE AND RESULTS OF RADIUM THERAPY IN MALIGNANT DISEASE. By M. DOMINICI, M.D., Paris, Chef du Service de Pathologie Interne, Laboratoire Biologique du Radium, and A. A. WARDEN, M.D., Glasgow and Paris, Visiting Physician to the Hertford British Hospital. Pp. 29, with 24 illustrations. Philadelphia: P. Blakiston's Son & Co., 1912.

THIS is a reprint from a report published in the *British Medical Journal* of August 27, 1910, of a clinical demonstration given by Dr. Warden for Dr. Dominici before the British Medical Association in 1910, with additional notes on the cases up to March, 1912. The report covers the results obtained by radium treatment of 9 cases of growths of a serious nature that were either inoperable or in which operation was declined. Reproductions from photographs of several of the cases are presented, showing the appearances before treatment and the admirable and really remarkable results obtained. Some of the reports are accompanied by reproductions of microphotographs of sections of the growths made before and during the progress of treatment.

H. K. P.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Experimental Production of Typhoid Bacillus-carriers in the Rabbit.—UHLENHUTH and T. MESSERSCHMIDT (*Deutsch. med. Woch.*, 1912, xxxviii, 2397) refer to the importance of bacillus-carriers in the spread of typhoid fever. As the gall-bladder is so frequently the depot of infection, it has been opened and drained in a number of instances, but the result is not always successful. By vaccine treatment uncertain results are also obtained; the bacilli disappear, only to reappear in a few months, as Uhlenhuth and Messerschmidt have been able to demonstrate. Chemical agents, such as chloroform, xylene oil, and potassium iodide, have likewise failed to inhibit the growth of the bacilli. The experimental therapy of bacillus-carriers cannot be properly undertaken until the conditions in man are reproduced in laboratory animals. By direct inoculation of the gall-bladder of rabbits, Uhlenhuth and Messerschmidt have succeeded in producing chronic bacillus-carriers experimentally. After six months the bacilli were still present in the gall-bladder. Such animals have been employed for experimental therapy; Uhlenhuth and Messerschmidt attempted immunization by vaccine and also employed chemical agents. By previous injection of vaccines they found it impossible to prevent the growth of typhoid bacilli in the gall-bladder of rabbits. Furthermore, rabbits which had been made chronic bacillus-carriers could not be cured by subsequent vaccination. Next, they employed a series of chemical substances but also without result. The substances used were iodethylhexa-methylentetramine, a mercury-atoxyl derivative, salicylate of copper, neosalvarsan, salvarsan, phosphorus, and colloidal mercury. Uhlenhuth and Messerschmidt found that the inflammatory changes in the gall-bladder of the rabbit were similar

histologically to those found in man. Occasionally they found that animals inoculated in the gall-bladder became sick and died with signs resembling those of typhoid fever in man, both clinically and anatomically. By reproducing the condition in animals, they have opened the way for a rational experimental therapy of typhoid bacillus-carriers.

On the Presence of Diphtheria Bacilli in the Urine.—R. KOCH (*Deutsch. med. Woch.*, 1912, xxxviii, 2356) has not found diphtheria bacilli in the urine of patients suffering with diphtheria as frequently as did Comardi and Bierast, who reported their presence in 54 of 155 cases. Koch examined 111 specimens of urine from 26 patients, and in 4 of these specimens from 2 patients he was able to cultivate organisms which were virulent when tested experimentally. In 10 other specimens from 5 patients suspicious organisms were cultivated by Loeffler plates, but it was either impossible to cultivate them in pure culture or they proved avirulent to animals. The virulent organisms were obtained in each instance from patients who died in the early stages of the disease from paralysis of the heart and vessels. Organisms similar to the avirulent diphtheroid bacilli were found in the urine 4 times out of 19 examinations of the urine of patients suffering with scarlet fever.

The Excretion of Formalin in the Urine after Hexamethylenamin (Urotropin).—Making use of the test for formaldehyde reported by Burnam, TALBOT and Sisson (*Boston Med. and Surg. Jour.*, 1913, clxviii, 485) examined 400 specimens of urine from 44 children. Practically all the acid urines contained formaldehyde, and the alkaline urines were negative. This was after hexamethylenamin by mouth. All of the 44 children tested showed formaldehyde in the urine at some time, while under observation. Hexamethylenamin is often excreted as such by children in alkaline or neutral urine, and is almost never broken down into formaldehyde, except in an acid urine. In some cases the dose had to be increased before formaldehyde appeared. Relatively large doses are frequently necessary. Inasmuch as the antiseptic power of urotropin depends upon the presence of free formaldehyde, urotropin should not be given with drugs that cause the urine to turn alkaline.

The Excretion of Formalin in the Urine.—SMITH (*Boston Med. and Surg. Jour.*, 1913, clxviii, 713) believes from observations that Burnam's test for formaldehyde in the urine is simple and accurate. It is definitely positive when formaldehyde is present in the strength of 1 part in 40,000 or more. A negative test at one time does not prove that formaldehyde is never liberated, after hexamethylenamin by mouth. The formaldehyde is liberated by the acids of the urine, not by a specific function of the renal epithelium. The process may take place in the kidney but is continued in the bladder. The degree of acidity of the urine, as measured by its hydrogen ion concentration, showed a constant relation to its power to set free formaldehyde. The higher the acidity, the greater was this power. In cases with persistently alkaline urine, Smith tried to change the reaction with

various drugs. Sodium benzoate, grains 15, t. i. d., had no appreciable effect; boric acid, grains 10, t. i. d., was effectual in several cases, but it is said to be toxic. Sodium acid phosphate given immediately after meals in $\frac{1}{2}$ - to 1-dram doses seemed more efficient than the other two, but may cause diarrhea. Among the fifty individuals whose urine was examined, there was only one case in which formaldehyde was never detected. As to dosage of hexamethylenamin, Smith feels that 5 grains does not lead to the appearance of formaldehyde in the urine, with enough regularity to warrant its routine use. Seven grains are followed by good quantities of formaldehyde lasting for six to ten hours. Ten grains every eight hours or 15 grains twice a day is the dose recommended.

Gastric Juice in Malignant and Non-malignant Diseases of Stomach and Duodenum.—SCHRYVER and SINGER (*Quarterly Jour. Med.*, 1913, vi, 309) conclude that there are no pathognomonic signs available in the gastric juice. No type of gastric juice is the exclusive or invariable accompaniment of any clinical condition. However, systematic gastric analysis helps to throw light on a number of pathological conditions. In the analyses Schryver and Singer, after a critical review of various indicators and methods, made use of the following: (1) For free hydrochloric acid: Dimethyl titration, appreciating that absence of dimethyl acidity may be due to either true achylia or a combination of secreted hydrochloric acid by amino-acid groups. (2) For "secreted" chloride: Subtraction from the total chloride of the chlorine determined in the ash after incineration (separation of the chlorine as hydrochloric acid and in combination with organic substances from the chlorine as sodium chloride). (3) For the peptic activity: The method of Fuld-Levison, apparently proving that pepsin secretion can be influenced independently of the hydrochloric acid secretion. (4) For the "nitrogen factor": The proportion of the difference between the titration value with phenolphthalein and that with dimethyl to the amount of nitrogen present as amino-acids, multiplied by ten. (In estimating the acidity of gastric juice to indicators, the amount of nitrogen present must be taken into account. In healthy gastric juice the "nitrogen factor" tends to approximate to figures 2.4. It seldom falls below, but with diminution of the digestive power it may rise greatly above. Schryver and Singer feel from their application of these tests that "secreted chloride" (*i. e.*, total chloride less inorganic chloride) is the best available index of gastric efficiency as regards hydrochloric acid. The latter, as it is secreted, enters either partly or wholly into combination with the products of digestion. The amount combined depends upon the amount and character of these products, index of which is furnished by the nitrogen estimations and the determination of the "nitrogen factor." In uncomplicated cases of duodenal ulcer, the amount of "secreted chloride" is raised, together with the peptic index, while the nitrogen factor approximates 2.4. The pyloric ulcers resemble these in general characteristics. Carcinoma of the stomach has no specific effect on the composition of the gastric juice, although both pepsin and chloride readings are generally lower than in other conditions. In alcoholism the peptic index is depressed, while the chloride

secretion remains normal. With visceroptosis and nephroptosis there is a general depression of the gastric functions. The "nitrogen factor" is raised. The same conditions prevail with atonic gastric wall. Hyperchlorhydria, hypochlorhydria, and even achylia are encountered independently by coarse gastric lesions. The coincidence of definite hyperchlorhydria with a greatly raised peptic index is practically diagnostic of pyloric and duodenal ulcer among gastric diseases. Very low chloride readings practically exclude pyloric or duodenal ulcer. A "nitrogen factor" of 2.8 and over has been found to be almost diagnostic of delayed emptying of the stomach. Dissociation of chloride and pepsin secretion is probably the result of chronic inflammatory change in the gastric mucous membrane.

Amylolytic Ferments in the Urine.—CORBETT (*Quarterly Jour. Med.*, 1913, vi, 351) has applied Wohlgemuth's method of quantitative estimation of amylolytic ferments in the urine to a variety of conditions. Normal individuals secrete a starch-reducing ferment in the urine, in the fairly constant amounts of 10 to 20 units on the average. Each unit represents 1 c.c. of 0.1 per cent. starch solution converted into dextrine in one-half hour by 1 c.c. of urine. A diet containing starch will increase the normal amylolytic ferment content of the urine. This was striking in the change from a milk diet to one containing much carbohydrate. Normal blood serum, by an equivalent method, showed the presence of the ferment with an average value of 10 units. As a direct measure of renal efficiency, Corbett emphasizes leakage of ferment requiring no renal activity for its elimination, and considers the relation of the serum-content to that of the urine of greater value than the urine content alone. When the value of the serum constantly exceeds that of the urine, it may be assumed that there is a considerable loss of renal efficiency. High readings in the urine were never found in pure cases of renal disease. All the cases of undoubted pancreatic disease, whether malignant or inflammatory, gave high values, and Corbett recommends the test as an aid in diagnosis of these conditions.

Effect of the Antityphoid Serum of Besredka upon the Course of Typhoid Fever.—The remarkable anti-endotoxic action of the serum of Besredka has been demonstrated. Even 9 fatal doses of endotoxin have been neutralized by a certain dose of serum. ANDRIESCU and CINCA (*Annales de l'Inst. Pasteur*, 1913, xxvii, 170) have studied the effect of the serum upon the course of typhoid fever, particularly upon the elimination of typhoid bacilli. The question was especially interesting to them as the mortality in Roumania varied from 10 to 20 per cent. compared to 6 per cent. of carriers. They chose 17 cases of typhoid from among the more serious types. In each instance they verified the diagnosis by hemoculture and Widal reaction. Serum was given subcutaneously in three or four consecutive doses, 40 to 500 c.c. in total amount. Two cases received serum intravenously. The serotherapy was in addition to the classical treatment of baths, intestinal antiseptics, liquids in quantity, etc. With one exception, a fatal case, they observed evident improvement in the general condition, but no definite effect upon the temperature. The most striking

result was the disappearance of typhoid bacilli from the circulating blood even twenty-four hours after the injection of serum. The effect was more marked after intravenous than subcutaneous injection. This fact certainly means an intense bacteriolytic action of the serum. To Andriescu and Cinca this alone justifies the use of the serum, and is of first importance in solving the question of carriers.

SURGERY

UNDER THE CHARGE OF

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Experimental Contribution to the Pathogenesis of Acute Hematogenous Osteomyelitis.—DUMONT (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxii, 116) says that it is possible to produce in young, growing rabbits, without trauma, by the intravenous injection of staphylococcus cultures, an acute hematogenous, suppurative osteomyelitis. The clinical picture will correspond to that occurring in man from the same affection. The cultures must have a hemolytic effect on rabbit's blood. For the production of a focus of osteomyelitis, cultures of the *Staphylococcus pyogenes aureus* as well as those of the *Staphylococcus albus*, may be employed. The variety of the organism employed is not of importance. It is merely the virulence which is of importance. The statement that a specific cause of suppuration, the bacillus of osteomyelitis exists (Hencke), is based upon error. Dumont's experiments, in which he produced osteomyelitis with the *Staphylococcus albus* developed from other sources of infection than osteomyelitis alone, proves sufficiently the error of this hypothesis. He believes that his experiments have succeeded in proving, experimentally, the interpretation of Lexer of the etiology of acute hematogenous osteomyelitis. Lexer supported it upon the basis of the anatomical arrangement of the bloodvessels of the bone and the biological properties of the staphylococcus. At the site of their deposit in the finest capillaries, chiefly in those of the metaphysis, these increased in number and thus became a focus of suppuration.

A New Method for the Diagnosis of Renal Tuberculosis.—BUERGER (*Jour. d'Urolog.*, 1913, iii, 431) says that he has demonstrated that the excision of a portion of the mucosa from the meatus of the ureter, can show the presence of miliary tubercles at a period when all other

evidence of renal tuberculosis is absent. Miliary tubercles may be present in this tissue, when the only visible change in the mucous membrane, even for the trained eye, is the appearance of "edema." The excision of this portion of the mucous membrane permits a positive diagnosis to be made, when it is impossible to use the ureteral catheter, when inoculations into lower animals prove negative, when the urine is completely clear, and when the disease presents practically no symptoms. In the beginning of the disease, in questionable cases of renal tuberculosis, a tuberculous focus can concentrate and localize itself at the meatal orifice of the ureter. Miliary tuberculosis may be found in the ureteral ostium even when the rest of the ureter is scarcely affected by tuberculous lesions and also when the pelvis of the kidney is only slightly affected. It will be necessary to practice this method of diagnosis when the objective findings are sufficient to permit one to suppose the development of a renal tuberculosis. It should be resorted to also when one fails to find the tubercle bacillus, and always when positive signs of invasion of the kidney by the tuberculous process are absent.

A Note on the Surgical Treatment of Calculus in the Lower End of the Ureter.—LEMOINE (*Jour. d'Urolog.*, 1913, iii, 441) did a transvesical operation for a ureteral calculus, which by the cystoscope and x-rays had been located at the vesical orifice of the right ureter. A mild Trendelenburg position was employed and the ureteral meatus was widened by a longitudinal incision. The calculus, however, could not be located. Then an iliac incision was made and the ureter exposed subperitoneally. It was found dilated to the size of the small intestine, and was progressively denuded to the kidney, which, as well as the pelvis, was distended in proportion to the rest of the ureter. Finally the calculus was located in the upper pole of the dilated kidney. Because of the pus in the urine and the thinness of the renal wall, the kidney and ureter were removed. The patient recovered. The calculus was 3 cm. long, 2 cm. wide, and 12 mm. thick, and weighed 13 grams. To determine whether the stone is movable or fixed, several methods may be employed: (1) Repeated skiagraphs may be made at intervals of several days, in varying grades of the Trendelenburg position. Change in the position of the stone in the different skiagraphs, indicates its mobility. (2) The ureteral catheter may be arrested and thus indicate fixation of the stone. But this method is open to error because a stricture or spasm of the ureteral muscle would produce the same result, or the catheter may pass to one side of the stone. (3) A skiagraph taken with the arrested catheter in position would show them both, and thus give strong presumptive evidence of fixation of the stone. Various methods of dislodging a fixed stone are mentioned. It may be approached for removal by the vaginal, rectal, perineal, or sacral paths, but these are not often employed. The transvesical and the subperitoneal are the paths usually chosen. When the stone is recognized to be movable, one may by endovesical methods try to provoke its spontaneous expulsion, or by inverting the patient, cause it to pass to the kidney, where it can be removed by pyelotomy.

Calculi in the Intraparietal Portion of the Ureter.—PASCUAL (*Jour. d'Urolog.*, 1913, iii, 147) says that calculi in the inferior extremity of the ureter have a characteristic and special symptomatology. They manifest themselves above all by vesical symptoms which lead one to think that the patient is suffering from cystitis. The cystoscope, generally, shows a ureteral orifice surrounded by edema. The skiagraph and ureteral catheterization will show with certainty the seat and size of the stone. The removal will be made by the natural path when that is possible, or by the suprapubic route if extraction by the natural path is impossible or has failed.

Consecutive Displacement of the Cerebral Hemisphere in the Localization and Removal of Intracerebral Tumors and Hemorrhages (Apoplectic Hemorrhages and Clots).—HUDSON (*Annals of Surgery*, 1913, lvii, 492) reports the case of a man, aged forty-five years, who had been in the hospital two weeks, with a slight paralysis of the right side, which had slowly progressed during this period. Hudson was called hurriedly at 2 P.M. On the previous day the patient had suddenly raised himself in bed, after which he grew worse with the symptoms of an intracerebral hemorrhage. He was entirely unconscious during the night. An operation was begun at 2.30 P.M., one-half hour after Hudson was first called, without ether. Oxygen would have been administered, but breathing had failed and artificial breathing was attempted. The brain was rapidly and freely exposed in the parieto-occipital region. An immediate backward displacement of the brain was observed; and the patient began to breathe. A hurried palpation of the brain showed a point which appeared more prominent than any other. Through this point the dura was incised, when immediately the cortex in the apex of a convolution ruptured; several clots of blood and a quantity of fluid blood were forcibly thrown out. At this point the patient's condition had so improved that more deliberation was possible. The hemorrhage from the cavity in the brain was quite profuse, but was eventually controlled with bits of dry cotton. The dura was not closed, and the finger of a rubber glove was caught with a stitch of fine catgut in the lower border of the dura. The brain at this point occupied its normal position within the dura, the abnormal tension produced by the hemorrhage having apparently disappeared. The bone flap was closed down and the scalp closed, the rubber drainage being brought out through an original trephine opening in the skull and the original incision in the dura. The hemorrhage was rather free for three or four days, and continued until the eighth, necessitating daily changes of dressing. The patient rapidly recovered, and was walking about the hospital from the fourth to the twelfth day, when he left. It is Hudson's belief that the surgery of the brain, which is the tap root of the tree of surgery, has failed to advance because of the surgical tools by which this surgery was attempted being inadequate for this work. He further believes that, with the thorough understanding and the proper application of this means, and by observing these methods of doing cranial surgery, the purely mechanical procedures are rendered as easy, quick, and safe as in abdominal surgery.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Pernicious Anemia.—BRAMWELL (*British Med. Jour.*, 1913, 2734, 1093) reports the results in 11 cases of undoubted pernicious anemia and in 1 doubtful case treated by salvarsan. Of the 11 undoubted cases, 4 have been apparently completely cured, but it is impossible to say whether a relapse will occur later or not. In 2 cases there was very striking temporary improvement, but ultimately they relapsed and death resulted. In 1 case there was slight improvement at first, but the patient died from bronchopneumonia while under treatment. In 2 cases there was no improvement, and in 1 case still under treatment there is slight improvement. Bramwell has had nearly forty years' experience with the ordinary arsenical method of treatment of pernicious anemia, and he believes that the salvarsan treatment is superior to the ordinary arsenical treatment. Further experience is necessary, however, before one can say whether the beneficial effects, which it undoubtedly produces in many cases, will be lasting or merely temporary. Bramwell has always given the salvarsan intramuscularly, the dose used being 0.3 gram, which is half the dose usually employed in syphilis. In view of the fact that pain and inflammation often follow intramuscular injections of salvarsan, he advises neosalvarsan, which does not produce such marked local reactions.

The Treatment of Diabetes with Rectal Injections of Sugar Solutions.—LUTHJE (*Therapie der Gegenwart*, 1913, liv, 193) reports good results from the administration of glucose solution to diabetics by rectal injection by the drop method. He says that the sugar is much better absorbed and utilized by diabetics when given in this way than when given by mouth. He has had especially good results in the treatment of acidosis by this plan. By the drop method, most persons can absorb from the rectum from one to two liters of fluid a day. He uses a 5.4 per cent. glucose solution, and hence the amount of sugar absorbed would be from 50 to 100 grams a day.

A New Protective Measure against Diphtheria.—VON BEHRING (*Deutsch. med. Woch.*, 1913, xxxix, 873) reports in detail his new method of active immunization against diphtheria. His preparation is a mixture of very strong diphtheria toxin and antitoxin combined in such proportion that the mixture shows only a slight, if any, surplus of the toxin when tested on guinea-pigs. The ordinary prophylactic measures against diphtheria have proved to be ineffectual and von Behring believes that this preparation is more efficient in producing

immunity against diphtheria than diphtheria antitoxin alone. He believes that one or more inoculations of his preparation will produce a protracted immunity to diphtheria and he reports cases that seem to support his views.

The Therapeutic Use of Strophanthin.—THORSPECKEN (*Deutsch. Arch. f. klin. Med.*, 1913, cx, 319) advises the intravenous injection of strophanthin in chronic cardiac insufficiency where other remedies are ineffectual or when gastro-intestinal disturbances prevent the use of the ordinary cardiac stimulants. Strophanthin is especially indicated in failure of cardiac compensation associated with congestion of liver and in contracted kidneys associated with dyspnea or edema of the lungs. Thorspecken advises the use of an initial dose of one-half of a milligram and twenty-four hours later a second dose of three-fourths of a milligram.

An Attempt to Interpret Present-day Uses of Vaccines.—SMITH (*Jour. Amer. Med. Assoc.*, 1913, lx, 1591), in conclusion, briefly summarizes the points to be emphasized in his article. He says that all parasites tend to increase the resistance of the host in which they live and multiply. Out of this universal fact a number of practical problems arise. In any given disease is it worth while to try to raise this immunity, and how much energy will it cost the patient? If worth while, what is the best and most sparing way of raising such immunity artificially? In any localized infection we must ask: Is this a beginning process without attendant immunity, or is it a residual process associated with general immunity? If the latter, vaccines may be considered safe. In processes associated with fever and bacteriemia, science says "hands off" until we know whether we have a progressive disease with gradual undermining of the resistance, or a more localized affection in which the excursions into the blood are secondary. In any case the use of vaccines in these cases must be regarded as experimental, and should not be undertaken save in conjunction with one trained in immunologic problems. Judged from this point of view as well as from the work of the laboratory as a whole, Smith believes that vaccines applied during disease will be rarely, if ever, life-saving, but they may hurry a stationary or languid process which tends toward recovery, by bringing into play the unused reserves of various tissues. The article is a valuable one and is very sane in its consideration of the proper application of vaccine treatment both for prophylactic and curative purposes.

Autogeneous Vaccines in the Treatment of Chronic Joint Affections (Arthritis Deformans and Gonococcal Arthritis).—HUGHES (*British Med. Jour.*, 1913, 2737, 1267) considers that so-called rheumatoid arthritis is a form of metastatic arthritis due to some primary focus of infection. The commonest foci of infection in Hughes' cases have been the teeth, especially pyorrhea alveolaris, the nose and nasopharynx, chronic otorrhea, the lungs, as a bronchitis or bronchiectasis, the intestinal tract, especially in diseases associated with stasis, and leukorrhea. In all such conditions the offending organism or organisms should be isolated from the primary focus and an autogenous vaccine

should be given for one or two doses. This raises the phagocytic powers of the patient, and it is then time to give the infected region the needed local treatment. If possible the primary focus should be removed. The use of the vaccines is to be persisted in for long periods of time if one is to succeed in the treatment. Hughes believes that chronic gonorrheal arthritis is due to a mixed infection with the gonococcus and staphylococcus, both of which can be cultivated from the interior of the urethra. A vaccine containing 100,000,000 gonococci and 150,000,000 staphylococci up to 500,000,000 of the former, and 1,000,000,000 of the latter is to be used, and after the second dose the chronic gleet is to be treated locally. Hughes has had very good results with this plan of treatment, but a complete cure often requires weeks or months.

The Diagnostic and Therapeutic Value of Intravenous Injections of "Arthrigonin."—BRUCH AND SOMMER (*Münch. med. Woch.*, 1913, ix, 1185) have injected arthrigonin intravenously both for diagnostic and therapeutic purposes. Arthrigonin is a polyvalent gonococcus vaccine that has been used successfully by intramuscular injection in the treatment of gonorrheal epididymitis and arthritis, but is not of diagnostic value when given by this method. Bruch and Sommer have injected the vaccine intravenously for diagnostic purposes, giving 0.1 c.c. of vaccine diluted to 0.5 c.c. with saline to men and 0.05 c.c. or less to women and children. Gonorrheal patients always reacted within forty-eight hours by a rise in temperature of more than 1.6° C. Non-gonorrheal patients showed much less reaction. No severe local symptoms occurred. For therapeutic purposes increasing doses were given intravenously at three- to four-day intervals, beginning with 0.1 c.c. and gradually increasing to 0.5 c.c. of vaccine. The patients treated improved rapidly and no injurious effect was observed. Various gonorrheal processes were treated with good results. Bruch and Sommer conclude that arthrigonin given intravenously is valuable both for diagnosis and treatment of any infection due to the gonococcus.

The Newer Theories in the Dietetic Treatment of Diabetes Mellitus.—TANSZ (*Med. Klinik.*, 1913, ix, 908) emphasizes the necessity of determining the point of tolerance for protein as well as for carbohydrates in each individual case of diabetes. In diabetes associated with nephritis, the diet should be regulated for nephritis as well as for diabetes and especially with regard to the tolerance for sodium chloride. The good results obtained from oatmeal and vegetable days is probably due to their increased alkali content and the consequent neutralization of acidosis. Tansz says that Abderhalden's researches have proved that albumin, fat, and carbohydrates develop protective ferments. Animal experiments have shown that it is possible for the body to produce ferments that aid in the splitting of the polysaccharides. In diabetes the metabolism is disturbed by an overaccumulation of carbohydrates, and if it were possible to increase the amount or the activity of soluble ferments the carbohydrates might be oxidized to a greater extent. Tansz says that experiments are being conducted with this idea in view.

OBSTETRICS

UNDER THE CHARGE OF

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The Immediate Treatment of Depressed Fractures of the Skull in the Newborn.—KOSMAK (*Bulletin of the Lying-in Hospital of the City of New York*, March, 1913) reports four cases of immediate operation for depressed fractures of the skull in the newborn. He employs a hook six inches long, inside measurement 3.16 inches, the inner side flat and at right angle to the shank. The point of the elevating hook is carefully introduced and turned at right angles to the surface so soon as the inner table of the skull has been perforated, and with these precautions no injury to the brain substance will occur. The point of the hook must be sharp enough to readily penetrate the skin, which has been previously sterilized before operating. Fractures of the fetal cranium may result without instrumental interference, and so the head of the newborn child should be carefully examined in all cases where there is reason to suspect unusual pressure. In every case seen by Kosmak where there was a depression in the fetal cranium there was also a fracture. The effort to use manual pressure to raise the depressed bone has not, in the writer's experience, been practical or successful. Force may be applied by this method to such an extent as to cause intracranial hemorrhage.

The Wassermann Reaction and Tuberculin Reaction during Pregnancy.—In view of recent studies in the blood serum of pregnancy, it is interesting to note the behavior of the pregnant patient in the Wassermann reaction and that occasioned by the use of tuberculin. DAUNEY (*Archiv. mensuelle d'Obst.*, April, 1912) reports the results of his studies with the Wassermann reaction in 82 patients, and 57 infants born of these mothers. He finds evidence that pregnancy inhibits the action of the Wassermann test in syphilitic women, for the result of the test was much more feeble and less pronounced than in syphilitic non-pregnant patients. He also finds that antibodies pass from the mother into the milk, and, in examining newborn infants, he finds that one cannot predict the reaction of the child from the reaction given by the mother. Women in florid syphilis giving a positive reaction to the Wassermann test may give birth to children having no sign of syphilis, but yielding a positive or partial Wassermann reaction. Syphilitic women giving a partial Wassermann reaction may give birth to children in whom the reaction is much more pronounced, while syphilitic women giving a negative reaction may give birth to children in whom the reaction is positive. Women suspected of syphilis, but having no sign of a negative Wassermann reaction may give birth to children giving a positive reaction. In suspected cases, where the Wassermann reaction is but faintly positive, or doubtful,

the child may be markedly syphilitic. Where the Wassermann reaction is negative, the fetal reaction is often doubtful. Cases are sometimes seen where women without a sign of syphilis, but who are suspected only of the negative Wassermann reaction, may give birth to a child having florid syphilis. In 21 infants, the Wassermann test gave identical results in mother and child in 9 cases; in 12 cases the reaction in mother and child did not agree.

In the *Monatsschrift f. Geburtshülfe und Gynäkologie*, Band xxxvi, Festnummer, 1912, BAR gives his results in the cutaneous use of tuberculin with tuberculous pregnant patients. This test was used to determine the prognosis and indications for the interruption of pregnancy. He found that, where the results were negative or very feebly positive, prognosis must be reserved when the tuberculous lesions seem to be localized. If the patient grew worse, without regard to the test, the safer plan would be the induction of labor. In pregnant women with pulmonary tuberculosis, without well developed lesions and well-marked tuberculin reaction, one would not induce labor because the lesions were not grave. Where a second test with tuberculin gives a very positive result when the first test was negative, the indication would be that the tuberculous process was extending rapidly, and the pregnancy should be terminated. The negative reaction, which was negative after the birth of the child, in the presence of grave lesions would indicate an approaching fatal termination.

Ovarian Pregnancy with Full Term Fetus.—Such a case is reported by GRIMSDALE (*Jour. Obstet. and Gyn. of British Empire*, February, 1913). The patient was a multipara, the heart sounds of the mother regular, the heart not enlarged, and the general condition fairly good. Upon examination, a hard, freely movable tumor about the size of a melon could be felt in the lower abdomen, reaching to the umbilicus. The tumor was not tender, was dull on pressure, and there seemed to be no free fluid in the abdominal cavity. Upon vaginal examination, the uterus was to the right of the tumor and not connected with it. The diagnosis of a solid ovarian tumor was made, and at operation this was found freely movable, with but one small adhesion. When the tumor was removed from the abdominal cavity it was found to occupy the position of the left ovary. The left Fallopian tube and mesosalpinx were normal, and the left round ligament could be traced to the uterus, and lay at the right of the tumor. The specimen removed consisted of the left ovary with the left tube and mesosalpinx. Upon opening the tumor, it contained a fetus and the placenta. An ovarian pregnancy was undoubtedly present. The centres of ossification indicated that the fetus had reached term.

The Immunology of Pregnancy.—MURRAY (*Jour. Obstet. and Gyn. of British Empire*, February, 1913) has made experimental studies to determine the question of immunology of pregnancy. While he analyzes his results, it is remarkable how little of it has a bearing on the relation of the normal to the toxic. To obtain definite knowledge, further results from the epiphanin reaction must be obtained. It was observed that immunity reactions were no strict measure of the immunity developed. With a proved immunity reaction in preg-

nancy, it is clear that all harmonal interactions, such as thyroid insufficiency, can be relegated to a secondary position. Toxic pregnancy naturally represents a defect in the production of the protective factors. Abderhalden's experiments appear to indicate that the prime error is in the placenta. The eclamptic placenta is unquestionably more toxic than the normal organ, although there is no positive evidence of a primary abnormality. The placenta, however, is almost as rich in enzymes as the liver. The indications are that in toxic pregnancy something is lacking which can be supplied by the addition of healthy pregnant serum, but in this the important element is the fresh character of the serum.

PETRI (*Zentralbl. f. Gynäk.*, 1913, No. 7) gives the results of his observations from the biologic diagnosis of pregnancy. He employed the blood serum from 23 pregnant hospital patients, and, by Abderhalden's method, made about 300 tests. These embraced all the months of gestation and the puerperal period after labor and abortion as well. He found the reaction positive as late as fourteen days after confinement. In 5 cases, it was positive from the first to the second day after abortion, and, in 9, from the first to the eighth day. He employed coagulated placental connective tissue obtained by boiling or cooking the placenta from which the blood had been removed.

Ileus Complicating Pregnancy and the Puerperal Period.—VAN DER HOEVEN (*Zentralbl. f. Gynäk.*, 1912, No. 46) has collected 94 cases of ileus complicating pregnancy and the puerperal period, and in 70 of these the histories give the cause, the treatment, and the prognosis. Adhesions were the cause in 35, and, of these, 24 were operated upon, with 13 recoveries and 11 deaths. The 11 which were not operated upon all died. Invagination was responsible for the accidents in 3 cases—1 operated upon, followed by death, and 2 recovering without operation. Volvulus was responsible for the condition in 13, 9 operations with 4 deaths, and 4 deaths without operation. Hernia in the anterior abdominal wall caused 2, 1 operated upon, followed by death, and 1 recovering without operation. Hernia in the broad ligament was the cause in 1 case cured by operation; in the mesentery in 1 case, dying after operation; in the diaphragm in 1 case, dying without operation. Epithelioma of the rectum produced 1 fatal case, without operation; stricture of the rectum, 1 of like nature; and ovarian cyst with twisted pedicle caused 3 cases operated upon, with recovery. Ovarian carcinoma was the cause in 1 case, recovering after operation. Posterior parametritis in 1, dying after operation. Hematoma in the pelvis caused 2, which recovered after operation; and retroperitoneal lipoma caused 1, dying after section. Incarceration of the retroflexed pregnant uterus was the exciting cause in 4 cases, 1 dying after operation, 2 dying without operation, and 1 recovering. Of 70 cases, 46 were operated upon, with a mortality of 46 per cent.; 24 were not operated upon, with a mortality of 81 per cent. In the remaining 24, constipation undoubtedly was the cause in 5; 1 of these died after operation, and 1 died without operation. In 15 fatal cases, autopsy failed to reveal any cause for the condition. Eight of these were not operated upon, and 2 died; 7 were treated by section, with 3 deaths. It is interesting to observe that even autopsy failed to reveal the

cause of the accident in between 15 to 20 per cent. of the cases. In view of the fact that many of these cases developed between the fourth and seventh month of gestation, and during the first day of the puerperal period, it seems impossible to believe that the pressure of the uterus on the intestine caused the condition. It is more rational to suppose that the pressure of the uterus against the bowel as it passes over the brim of the pelvis, was an important factor. When the vagina is not distensible at the third or fourth months as the uterus expands, traction is made upon the cervix, and the cervix is drawn up into the pelvic brim. This was well illustrated in a case treated by section in the third month of gestation. Contracted pelvis makes this pressure at the pelvic brim more pronounced, and the accident has occurred in these cases after delivery by symphysiotomy or Cesarean section. The presence of myomatous tumors of the uterus also predisposes.

GYNECOLOGY

UNDER THE CHARGE OF

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Treatment of Uterine Hemorrhage by the Galvanic Current.—JAMOULLE (*Gaz. de Gynéc.*, 1913, xxviii, 49) says that uterine hemorrhages may be roughly divided into three groups, according to their etiology: (1) Those due to altered ovarian secretion, (2) those due to pathologic conditions of the endometrium, and (3) those due to alterations in the uterine *parenchyma*, *i. e.*, to atonia or insufficiency of the uterine muscle. The latter group, and these alone, are amenable to treatment by the constant galvanic current, the effect produced being dependent upon the well-known action of this form of electricity in causing contractions of smooth muscle. Cases of subinvolution, of profuse hemorrhage at puberty or the menopause, without demonstrable lesion, or associated with a sclerotic condition of the uterine walls, the result of long congestion or of chronic inflammatory processes, are the ones usually most benefited by the galvanic current; in these it appears to exert an excitomotor and trophic action upon the muscle fibres, whereby their tone is restored and their contractility increased. In a few cases of fibroid tumor, where operation is definitely contraindicated on account of tuberculosis, renal or cardiac conditions, the use of electricity may be justifiable, as well as in the case of patients near the menopause suffering with fibroid tumors, or of young women with small tumors, and desirous of having children. An absolute contraindication to this form of treatment is furnished by the presence of acute or chronic adnexal inflammation, since the excitation of the tubal musculature produced by it may lead to disastrous consequences. If the first electrical treatment is followed by a rise in temperature and pain in the adnexal regions, no further trials with it should be made,

even if the most careful palpation fails to reveal the presence of tubal masses. The technique is comparatively simple. Any ordinary medical battery furnishes the current. The positive pole consists of a sound of non-oxidizable metal (nickel, platinum), which is ordinarily introduced into the uterine cavity, and is surrounded by an insulating cuff to protect the vaginal walls. The negative electrode consists of a plate of metal wrapped in moist cotton, placed on the suprapubic region of the abdomen. A constant current is used, of from 50 to 60 milliampères; in rare instances this may be gradually increased to 150 milliampères. The sittings last from eight to ten, or occasionally fifteen minutes; they are given every other day, or even daily. As a rule, six to eight treatments are sufficient to produce the desired result. In some instances, especially in hemorrhages of congestive nature, vagino-abdominal galvanization appears preferable, the positive pole being placed in the posterior vaginal vault instead of in the uterine cavity. In this case it is necessary to wrap it also in wet cotton, to avoid injury to the vaginal walls. In applying the treatment to young girls it is usually possible to avoid even intravaginal application, one pole being placed over the lumbar, the other over the pelvic region, a method which Jamouille has found to give sufficiently satisfactory results in these cases.

Extirpation of the Bladder.—Two rather remarkable cases of almost complete resection of the bladder are reported by NICOLICH (*Folia Urologica*, 1913, vii, 371). Relying upon the work of Schwartz, who found that in dogs resection of the entire bladder except the trigone was followed by the formation of a satisfactorily functioning organ, Nicolich performed his first operation upon a patient, aged seventy-two years, who was suffering from a papillary, infiltrating carcinoma, involving the entire bladder wall with the exception of the trigonal region, which was free. After resecting the entire bladder, with the exception of this portion, he closed the peritoneum with cat-gut, and sutured it to the upper angle of his abdominal incision. He then brought the remaining portion of the bladder walls together as well as possible, but was not able completely to close the opening; a large tampon of iodoform gauze was, therefore, placed between the bladder and the peritoneum, and a second, smaller one directly over the bladder. The abdominal incision was left entirely open. The patient stood the operation well (spinal anesthesia); by the fifty-second day the wound had entirely closed, and micturition was normal, occurring about every three hours. Two months later the patient was able to return to work; a radiograph taken at this time, after the injection of 100 c.c. of collargol, showed the new-formed bladder in normal position, with a small diverticulum. Ten months after operation the patient was still enjoying the best of health. The second operation, practically identical in nature, was performed for multiple papillomas, which two previous cystotomies had failed to cure. In this instance the wound was closed by the twenty-second day; the patient urinated every two hours during the day and every four hours at night. A collargol radiograph two months later showed a somewhat larger and more regular cavity than in Case 1.

DERMATOLOGY

 UNDER THE CHARGE OF

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The Treatment of Carcinoma of the Skin with Carbon Dioxide Snow and the X-rays Combined.—FABRY (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 2), finding that previous freezing of carcinomatous lesions lowers their resistance and makes them more readily influenced by the x-rays, employs the following combination in the treatment of such lesions, which he regards as superior to all other methods. The carcinoma is first frozen for one minute, then allowed to thaw completely and again frozen for a minute; it is then x-rayed immediately or after one or two days, four-fifths of an erythema dose being given. Under an indifferent salve healing takes place within two to four weeks, the length of time depending upon the size of the lesion. Of 12 cases treated in this manner complete healing was obtained in all but 1, in most instances with scarcely perceptible scarring.

The Experimental Production of Pellagra in the Monkey.—HARRIS (*Jour. Amer. Med. Assoc.*, June 21, 1913) has succeeded in producing in the monkey symptoms resembling human pellagra by employing subcutaneous, intravenous, and intracranial injections of a Berkefeld filtrate made from pellagrous human tissues. The first monkey injected remained apparently normal for many months, but eventually developed an eruption consisting of dark patches situated on the face, upper extremities, and trunk, and finally died with all the signs of pellagra. A second monkey which was given two injections two months apart, five months after the first injection showed scaly eruption of a dusky red color on the face, ears, and backs of the hands which itched. This monkey likewise developed a slight diarrhea and considerable salivation. Microscopical examination of the skin of the first monkey showed a picture identical with that presented by the skin in human pellagra. Harris believes the result of these experiments indicate that pellagra may be transmitted to the monkey by a Berkefeld filtrate made from pellagrous human tissue, and that the cause of pellagra is a filterable virus capable of passing through the Berkefeld filter.

A Tuberculide Resembling the Lichen Planus of Wilson.—VIGNOLO-LUTATI (*Annales de Dermatologie et de Syphiligraphie*, 1913, No. 4) reports the case of a woman, aged twenty-five years, who presented an eruption, situated exclusively upon the backs of the hands and the extensor surfaces of the lower third of the forearms, consisting of papules presenting the characters of lichen planus. The papules were pink or violaceous, with smooth shining surface, and in some instances showed a minute umbilication. The eruption was not accompanied by any subjective symptoms. The patient likewise presented the

symptoms of pulmonary tuberculosis and, in youth, had suffered from a scrofulous adenitis the scars of which were still visible in the neck. Microscopic examination of sections of excised lesions stained by the method of Weiss revealed a small number of tubercle bacilli. This case was in all essential features like the one reported by Bosellini, in which tubercle bacilli were also demonstrated.

Studies in the Metabolism of Some Diseases of the Skin.—NEIDITSCH (*Archiv f. Dermatologie u. Syphilis*, Band cxvi, Heft 1) studied a series of 41 cases of various diseases of the skin, such as psoriasis, ichthyosis, dermatitis, herpetiformis, dermatitis exfoliativa, acute and chronic eczema, urticaria perstans, urticaria pigmentosa, for the purpose of determining whether there was a greater increase than normal in the excretion of the amino acids, i. e., whether there was a disturbance in albumin catabolism, regarding these acids as the most characteristic elements of the albumin molecule. His investigations led to practically negative results, since in none of these diseases neither—in psoriasis, eczema, nor ichthyosis, could an increase, of pathogenetic significance, be demonstrated; nor was the quantity of amino-acids contained in a spontaneous bleb of pemphigus vulgaris increased. GEBER (*Dermatologische Zeitschr.*, Band xxii, Heft 5, 1913), in a study of the nitrogen and sulphur metabolism in psoriasis found, contrary to the conclusions of Haemerli recently published, that with a constant weight of nitrogen there was no increase in the excretion of sulphur in psoriasis. The variations in the sulphur excretion which he observed in his cases stood in close relationship to the increase or diminution of nitrogen intake. Although an increase in the sulphur excretion in proportion to the intake was noticed with a nitrogen-poor diet, he did not regard this as at all characteristic of psoriasis.

Mycosis Fungoides Successfully Treated by Hypodermic Injections of Arsenic.—WOLFF (*Archiv f. Dermatologie u. Syphilis*, Band cxv, Heft 9) at a meeting of the Strassburg Dermatological Society, December 15, 1912, exhibited a case of mycosis fungoides which had been successfully treated by injections of atoxyl and arseniate of soda. The patient was a man, aged thirty-three years, who, in 1907, had an eruption scattered over the whole body consisting of irregularly-shaped, elevated, partly scaly, partly papillomatous areas with polycyclic borders, accompanied by moderate itching. After seventy injections of atoxyl (dose not mentioned) complete healing took place, and the patient remained well until 1910 when two lesions appeared upon the chin like those above described together with a fungoid tumor with broken-down centre upon the sole. Injections of arseniate of soda in ascending doses up to 0.03 per day, with x-ray treatment of the foot, produced complete healing in six weeks. The exhibitor also presented photographs of two other cases of mycosis fungoides successfully treated in the same manner.

Erythema Nodosum and Tuberculosis.—POLLAK (*Wien. klin. Woch.*, 1912, No. 32) in 48 cases of erythema nodosum occurring in children obtained a positive tuberculin reaction in every case. He is therefore of the opinion that erythema nodosum is probably a

tuberculous affection of the skin. SEZARY (*Medical Press and Circular*, 1912) calls attention to the fact that many children with tuberculous meningitis have previously had an attack of erythema nodosum.

Multiple Pigmented Warts in Pregnancy.—WARD (*British Jour. Dermat.*, May, 1913) records an unusual and annoying complication of pregnancy. A healthy brunette, aged twenty-three years, became pregnant for the first time, and in the later months of her pregnancy was greatly annoyed by the appearance of a crop of pigmented warts on the trunk, neck, and limbs; with the termination of the pregnancy a few of the warts disappeared, but the majority remained. Four years later the patient again became pregnant, and at the end of the fifth month a new crop of warts appeared over the body and extremities, avoiding the face and hands. Unlike in the previous pregnancy, none of the warts came off with the birth of the child.

The Treatment of Epithelioma of the Lip by the X-rays.—PUSEY (*Jour. Cutaneous Diseases*, February, 1913), while not advocating the substitution of the x-rays for radical surgical measures in the treatment of epithelioma of the lip, believes that, in selected cases it is capable of producing results which compare favorably with those obtained by purely surgical methods. In support of this opinion he presents the following statistics: From 1901 to 1909, 44 private cases of epithelioma of the lip were treated by the x-rays. Six of these are for various reasons left out of consideration, leaving 38 cases, 35 of the lower lip, and 3 of the upper. Of these 38 patients 28 were living and well in January, 1912. Two of the patients had lived nine years; 7, eight years or more; 7, seven years or more; 5, six years or more; 2, five years or more; 5, four years or more; and 8, three years or more. The percentage of failures was only 5.25.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Action of Arsenic in the Anemic.—SANEYOSHI (*Zeitschr. f. Path. u. Ther.*, April, 1913, xiii, 1) details his observations in pursuance of the knowledge of the way in which arsenic acts on the cure of anemia. He has observed the morphological changes in the blood of dogs during the administration of arsenic, and by oxygen-estimation, the degree of regeneration; finally he has compared the iron content of the liver and spleen with the normal. Arsenic in large toxic doses causes hemolysis and a corresponding anemia, for the repair of which regeneration at once proceeds. In smaller doses,

though still relatively larger than those in ordinary therapeutic use, no anemia occurs, and no marked change is to be observed in the blood. There appeared no unusually rapid disappearance of corpuscles nor any unusually prompt replacement of such corpuscles as had disintegrated. Oxygen analysis verified these observations, and forms a very accurate mode of estimating the variability of young corpuscles in the circulating blood. No regeneration beyond normal limits seemed to occur, nor was hemosiderosis demonstrable in the liver and spleen. Bettmann, and later, Kuhn, consider that arsenic does not directly stimulate the blood-forming organs but causes a peripheral hemolysis, and the consequent lack of oxygen becomes or causes the stimulus to bone-marrow. Saneyoshi thinks this untenable, but does not go further than to suggest that arsenic is especially potent upon cells that are young and strongly proliferative.

Experimental Myocarditis from Rheumatic Sources.—BINDO DE VECCHI (*Arch. de Med. Exper.*, xxiv, 352) undertook the blood examination of rheumatism, but found his cultures from the blood stream to be sterile. He then injected the serum of such blood intravenously in dogs and rabbits; to the naked eye this was followed by no result, but microscopically there resulted areas of cellular infiltration, of general distribution, but most evident in the papillary muscle, and chiefly perivascular. The cells are sometimes of one kind, sometimes of various sorts, lymphocytes, leukocytes, and plasma-poor cells with large nuclei; subsequently fibrotic processes appear. Four cases out of five showed these areas, which were never found in control animals. Blood from persons sick of nephritis, polyneuritis, and tuberculosis showed lymphocytic areas with slight muscular degeneration; but the author has not regarded them as specific, as are the areas under consideration. They bear great likeness to the so-called "rheumatic nodules" observed in the heart muscle of persons dead of rheumatic fever. Their situation in the myocardium makes it seem probable that extension could readily occur to endocardium and pericardium. De Vecchi's next step would naturally be to use the Berkefeld filter upon such serum, and to verify his interesting observations by larger series of animals.

Recurrent Fever.—During the course of study upon exanthemic typhus, NICOLLE, BLAIZOT, and CONSEIL (*Annal. de l'Inst. Pasteur*, March, 1913, xxvii, No. 3) were enabled to make some interesting observations with regard to recurrent fever, namely, that it is transmitted by lice. It may be said with regard to exanthemic typhus that the local name in Tripoli is translatable as "the louse disease," a term which has its purpose in an attempt at prophylaxis. The louse has for some time been suspected of being the transmitter of recurrent fever, and the chief reason against admitting the truth of this supposition was that lice nourished upon men or apes suffering from disease were unable to cause the disease in others by biting. When examining lice which had bitten patients suffering from recurrent fever, it was found that there was a rapid disappearance of the spirilla from the body of the insect; but prolonged observation showed that this disappearance is only apparent, for after a delay of eight days

they reappeared and persisted for a couple of weeks before they again disappeared finally. The spirilla after their reappearance are virulent for man and ape. They are localized to the lacunar cavity, and do not invade the apparatus of the mouth or the digestive tube. Shut off from communication from the outside, as long as the louse remain alive, they perish with the death of the insect. A simple bite does not, therefore, infect. One victim, whether human or Simian, had as many as 6500 bites inflicted upon him without becoming infected. It is when the body of the louse is crushed and the skin excoriated by the nails at the same time, that the lacunar liquid escapes, and inoculation occurs. The head louse and the body louse are both efficient causes of the disease. The infection is preserved, doubtless, through the various generations of the insect, and each variety of acarus has apparently its own variety of spirillum.

Transplantation of Tumors upon an Embryo.—J. B. MURPHY (*Jour. Exper. Med.*, April 1, 1913, xvii, No. 4) has obtained some wonderfully striking results in inoculating rat-sarcoma into developing chick embryos. It is at the present time difficult to correlate all the various observations that have been made tending to show the specific nature of tissues in their behavior one to another. There was recently shown in the *Journal of Experimental Medicine*, by Rous, a striking example of the strictness of the laws of specificity; chicken sarcoma failed to grow in any other chickens than blood relations of the host in its first transfers; later it would grow in any animal of the same breed, and ultimately, when its malignancy had been much enhanced, it would grow in chickens of other breeds. Some have supposed that there is in the body of the host an immunity reaction against the foreign cells; others have thought that the host lacks some specific food substance which is necessary for the growth of the grafted material. Briefly, Murphy was able without difficulty to obtain tumors in the embryos, or in the membranes, and was able to carry the inoculation from embryo to embryo indefinitely. During long life in a new host, the rat cells showed no change in their morphology, nor any loss in their ability to produce characteristic tumors when transplanted back into the rat. When placed in the adult chicken tissues, the embryo-nourished cells died even more quickly than cells taken direct from the rat, so that they appear to have gained no adaptation to the new species. Murphy has succeeded in implanting various embryonic cells from the chicken, mouse, and rat, as well as various other sarcomas, chondromas, and carcinomas, upon the embryos.

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ORIGINAL ARTICLES

THE INFLUENCE OF SKELETAL DEFECTS, CONGENITAL AND
ACQUIRED, UPON THE BODY IN HEALTH AND DISEASE.

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AMONG the many good results attained in the period of specialization through which we are passing has been the focusing of attention upon certain of the fundamental branches of knowledge necessary for a physician to possess. Little by little it has been found that many of the old theories in regard to disease were erroneous in whole or in part, and research has supplied in some instances at least a correct theory upon which to work. Much has still to be learned. Not all the problems are as yet solved. Scarcely a month goes by without some promising clue being discovered, and though most of them do not lead to the desired result, still the following of them up is bringing us a little nearer the truth. It seems strange sometimes that anatomy should be the branch of medicine to which we may still look for suggestions in the solution of our problems. It has been the groundwork of a physician's knowledge so long that it would appear at first thought it could have no secrets that had not already been revealed. Viewed from the standpoint of descriptive anatomy alone it is probable that there is not much to be added to what has been observed from the time of Vesalius to our present-day authorities. There is, however, another side to anatomy, and that is the comparative. The human being, as we study him, is looked at as the product of an evolutionary process operating through an immeasurably long period, and it may well be that we are still in a transitional stage. Environment and its necessities have imposed upon the

evoluting creature, whatever it may have been, its impress. Adaptation to its surroundings has been a characteristic of a developing organism, whether we look upon the life history of an individual or of the race to which he belongs. Some of the functional adaptations are trivial, and others are more or less fundamental. Looked at from this standpoint it would seem that anatomy might still have many a lesson for us which should be valuable in preparing the way for a better understanding of some of our unsolved problems. In what is to follow, therefore, there will be presented to a considerable extent some of the attempts to profit by knowledge acquired from anatomic sources.

We are disposed to assume that the body is so endowed with energy and is so infinitely adaptable to changing conditions that its functions may be continued in a normal manner to permit of healthful existence and the output of a volume of energy proportioned to the capacity of the machine. It is true that in the human mechanism there is a wider latitude than there is in any other known mechanism for loss of force and for the performance of function under conditions which are, to say the least, adverse. What we do not realize, and have taken few steps to understand, is (1) to what extent anatomic defect influences the proper functional uses of the body; (2) to what degree and in what way these anatomic peculiarities may influence physiologic function; (3) to what kind of abnormal anatomic changes these perversions of function may give rise.

The history of the practice of medicine is replete with examples of the way the profession has tried to solve situations where anatomic disarrangements seemed to be the cause for a train of symptoms physically distressing to the patient. One need only mention the fact that a considerable part of gynecologic treatment has had such a supposition as its basis, and the fact that floating kidneys and other visceroptoses have been treated mechanically by the surgeon with this hypothesis in mind. Pain or some form of physical discomfort is the factor that leads a patient to seek advice from his physician in the majority of cases, and in the procurement of a total or partial relief of this both patient and physician lose sight of the underlying cause of this symptom and of effects which are oftentimes of more real significance than the pain itself. A more thorough knowledge and appreciation of the interdependence of physiologic function upon anatomic adaptation to environment and function is what is needed on the part of everyone who seeks to aid in the solution of medical problems in these days.

The results of the researches of laboratory investigators in the past twenty to thirty years have brought us to a position where a large part of the diseases which we are called upon to treat have been shown to be the result of infections. In those cases in which it has been possible to isolate and specifically identify the cause

of an infection we are content for the present at least to assume that this is the prime and essential source of the disease and devote ourselves to the problem of trying to produce a vaccine with which to treat it. In certain conditions, however, we cannot isolate a specific bacteriologic cause for symptoms which in themselves are suggestive of infection, and we are forced to fall back upon what we designate autointoxication and assume that there is some undiscoverable source of infection in the body. In certain of this latter group of cases we are coming to the conclusion that anatomic visceral defects are capable of setting into operation faulty functional processes within the abdominal cavity, and that the patient becomes poisoned by the consequent interference with the machinery by which he should be rid of his waste physiologic products. In these cases nothing is brought in from the outside that was not already there, as has been assumed to be the case in the first-mentioned group; but we must not lose sight of the fact that we have no satisfactory scientific explanation of what the factor is that must be present beside the infecting organism to make possible the development of any infectious disease. We satisfy ourselves by saying that this factor is lowered resistance. If we are honest with ourselves we can recall innumerable instances where we have looked long and in vain for any evidence of such lowered resistance in cases where there has been no question about the infection. Flexner has recently shown that the organism which was capable of causing anterior poliomyelitis in a monkey was being carried in the nasopharynx of the healthy parents of a child who was then going through an attack of this disease without causing any symptoms in the hosts. Arbuthnot Lane is performing as a routine measure an intestinal short-circuiting operation in all children with bone tuberculosis, on the theory that visceroptosis in some of its forms is the cause for these infections. Indefensible as this position of Lane's seems to many of us it may well be that the lesson we should learn from it is that we must be on the alert to discover in some anatomic lack of adaptation the link that is so often missing in furnishing a complete explanation of the phenomena of infectious disease. If as time goes on such interrelationships should prove to be of frequent occurrence and others should be discovered not now even suspected, our whole plan of attack upon disease as the enemy of mankind will of necessity have to be remodelled. Numerous suggestive interrelationships between functional disturbances in the special senses dependent upon primary anatomic defects in one of the special sense organs might be cited as in line with this suggestion. Disturbances in the function of certain of the ductless glands give rise to serious upsets in the metabolism of the body, causing disarrangements in the functional activity of organs having at least no direct anatomic connection with the gland in question. What it was that was directly

responsible for throwing the gland out of its proper functioning we are not in a position to say. Anatomic obstacles may reasonably well be looked to in explanation of a lack of functional adaptation here as elsewhere.

It is time, therefore, that all the knowledge which these years of activity on the part of trained clinical observers in special fields have accumulated, together with the results of laboratory research along physiologic and pathologic lines, should be made to converge upon the accumulation of anatomic data in our possession, which must be the foundation stone upon which every scientific conception of disease must rest. We must get away from the notions which have so strongly dominated our thought in the past, based upon a dead pathology. To be of help to us our pathology must be a living pathology and we must realize that most of the diseases which flesh is heir to are the result of perverted physiology. I believe that in the future we shall discover that anatomic defects, either congenital or acquired, will be at the root of physiologic perversions more often than we now appreciate.

Certain of the anatomic skeletal disarrangements have been carefully studied and some suggestive light has been thrown upon a type of joint trouble which Preiser has classed as static joint disease and about which he has written extensively.¹ He groups the joints under the heading of static units and shows how any defect in any member of a static unity causes every other member of that unity to suffer. As an example of how this works out he refers to the influence of a pronated foot or a knock-knee upon other parts of the static unit of which the foot and leg are members. So also in the arm he refers to the effects of a cubitus varus upon the shoulder girdle and the carrying function of the arm. He speaks of the effects upon the joints of a static unity in the way of interference with the use of the articular cartilages as an "incongruence," and says that the results of these incongruences are expressed through changes in cartilage, bone, and circulation, producing, as a terminal effect, disturbances in the nutrition of the joints. He points to the fact that these same disturbances or incongruences may be produced in joints as a result of old healed diseases, for example, tuberculosis, infectious arthritis, and juxta-epiphyseal osteomyelitis. Again, he shows that variations in the anatomic types of the pelvis, by rendering the normal bearing of the femoral head against the acetabular floor impossible, cause "incongruence" of the bones at the hip- and knee-joints which lead to permanent anatomic changes, interfering with function and giving rise to the symptoms of arthritis. It is impossible that such a condition as this in the pelvic girdle should exist for long without its giving rise to such disarrangements in the

¹ Amer. Jour. Orth. Surg., vol. x, No. 1.

relationships of the lumbar and low dorsal vertebræ to each other that they in their turn should not manifest similar evidences of "incongruence" of articular surfaces, limitation of motion, and impairment of function. The significance of these primal anatomic defects is enhanced if there is coincidentally present an inherited tendency to a diathesis such as that commonly denominated hypertrophic arthritis. In the shoulder girdle, whether from postural errors or anomalous development, we frequently meet with symptoms referable to the hand, forearm, shoulder, and cervico-dorsal spine, which are due primarily to anatomic disarrangement of this "static unit," and as a result of this there develop nerve-root compressions, articular "incongruences," continuous strains upon ligamentous and muscular structures, which are of themselves painful, and result in impairment of function. Any one of the above-mentioned phenomena is of itself more or less distressing, and will, if permitted to continue, eventually exercise a harmful influence upon the patient as a whole.

In the feet one is constantly brought into contact with patients who for one reason or another have neglected to give attention to minor static defects. The congested, swollen, and painful foot, which is normally flexible in spite of static defects, readily passes over into the rigid, contracted foot, in which there are articular "incongruences" and serious disability.

Preiser has grouped the symptoms of the statically diseased joints under three heads: (1) Difficulty in getting the joints to work easily and comfortably after prolonged rest; (2) relief from this difficulty after being limbered up; (3) renewal of pain and stiffness after prolonged use.

F. H. Martin,² in an article entitled "Perpendicular Pelvis," has called attention to anatomic anomalies of the bony pelvis which he believes to be a cause for the development of certain gynecologic difficulties.

Further citation of examples of this cause for symptoms having no other primal explanation than anatomic defect is hardly necessary for the purposes of this discussion. It will be noted that among these conditions which have been mentioned some are of congenital and some are of acquired origin. It is probable that under the right conditions and during the earlier periods of life faulty attitudes and the assumption of an habitually poor poise, whether sitting or standing, may graft upon the individual methods of the employment of the various muscle groups which permanently impair their efficiency, bring about faulty skeletal relations, and render difficult the application of the energy of the growing child to the activities which are an essential part of its growth and development. Even the superabundance of animal spirits, which

² Jour. Amer. Med. Assoc., July 29, 1912

is the heritage of the normal child, cannot overcome indefinitely the handicap imposed by skeletal incongruence, and many a case of physical incapacity and deterioration can be traced to this alone.³

If the old aphorism that "as the twig is bent so the tree inclines" has any application here it is evident that the time to prevent the more serious handicaps of adult life, which are of this character, is before the changes which render the figure incapable of remodeling have taken place. It is important that those who are custodians of the health, the physical efficiency, and mental vigor of the race should realize that the prime reason for insistence upon good carriage in youth is not for the sake of the appearance one makes, but for the absolute dependence of all, except the expressly endowed in these respects, upon their being able to meet the world without physical handicap.

Recently Dr. J. E. Goldthwait⁴ has drawn attention to still another series of congenital skeletal anomalies that seem to have considerable significance. These are situated within the narrow limits of the pelvic girdle, including the last of the lumbar vertebrae. Here are anatomic structures capable of such disarrangement, either congenital or acquired, that they may give rise to physical incapacity and discomfort of considerable significance, and this without complication by any of the pathologic conditions common to bone. Some of these are the result of anomalies in development hitherto not supposed to have any clinical importance.

The primal condition of the progenitors of the human race was that of a creature whose progression was, in whole or in part, upon "all fours." To have evolved from this anatomic skeletal entity a creature whose progression is upon the posterior two of these original four legs has entailed considerable skeletal modification extending over periods of time which are almost inconceivable. The necessities of adaptation to a changing environment and to changing conditions of existence have been responsible for the varying degrees of conformity to a normal standard observed in various parts of the bony skeleton. Evolution in the osseous skeleton is progressing just as it has been in other and more thoroughly studied parts of the body, and the perfect adaptation of the body as a whole and in all its parts to the requirements of function and environment has not yet been attained. Until that period it is probable that we shall be obliged to employ our ingenuity and thought in trying to find some way to overcome the failure of the slow plodding evolutionary processes to meet the physical necessities of the organism.

One of the regions where the greatest evolutionary change has taken place in transforming a quadruped into a biped is at the

³ The Relation of Posture to Human Efficiency, J. E. Goldthwait, M.D.

⁴ Boston Med. and Surg. Jour., March 16, 1911, pp. 365 to 372.

junction of the pelvic girdle with the trunk. Here there had of necessity to be very great modification in the coarse as well as in the fine adjustment of the parts. Here we find considerable variation in the size, shape, and alignment of skeletal structures. When the pelvis was adapted to sustain the weight of the posterior part of the body at right angles to the method of the biped and the muscles originating on the pelvis and operating the legs exerted their stress in a manner not now employed the inclination of the pelvis was different, and the way in which many of the articular facets inclined as well as their shape had of necessity to undergo modification. Between the four-legged progression of remote quadruped ancestry and the present human carriage there was developed the monkey, whose method of progression was in part one and in part the other, that is, in part quadrupedal and in part bipedal. A pronounced modification of the pelvic girdle had of necessity to be made in order to make such a dual method of progression possible. Now in man we have departed so far from a pelvic development of the type that prevails in the monkey that man could not if he chose, except in the earliest years of life, progress in any other way than on his "hind legs."

The sacrum varies greatly in size, in shape, and in the inclination with which it meets the other pelvic girdle bones. Besides these gross variations there is a variation in the shape and inclination of the articular facets. There are wide variations in the last lumbar vertebræ. In some cases the fifth lumbar has been sacralized; in others the transverse processes of the fifth are so long that they impinge upon the sides of the ilia. They are bent upward in some cases. At times there is an articulation between the tip of the transverse process and the ilia or there may be a joint between the inferior surface of the fifth transverse process and the sacrum. In still other instances there are bursæ between these fifth lumbar processes and the sacrum or the fifth and the ilia. Another anomalous situation is seen where the fifth lumbar and the sacrum are fused. This may be the case on one side, whereas on the other there is the normal anatomic condition. In some specimens there is a wide variation in the size, shape, and inclination of the articular facets on the fifth lumbar, with corresponding changes in the sacral articular processes. In those variable anatomic relations one finds the possibility of various disturbances, some of which are purely static and others are the sequels of primarily static arrangements.

We have here in this small compass the potential of sprains of articulations between the facets holding the last lumbar upon the sacrum as well as between the supernumerary joints which may exist between the sacrum and the transverse processes of the fifth lumbar and the fifth lumbar and the ilia. Also bursal irritation in bursæ located as above described. Because of the departures

from the normal in the size and shape of the articular facets occasionally there are dislocations or luxations of these facets with the signs of such anatomic disarrangements added to the signs of sprain. Furthermore, the posterior nerve roots making their exit below the transverse processes of the fifth lumbar may be compressed by the disturbed relationships of the sacrum and the last lumbar, sciatic symptoms being thus produced. Accompanying such static disarrangements we may find evidence of various arthritic lesions, notably the hypertrophic type and other non-tuberculous forms of infectious arthritis, more rarely tuberculosis. Associated with many of these lumbosacral strains the sacroiliac articulations may be involved, especially in those where the cause is one which has operated over a long period of time.

It is a specious form of logic which seeks to draw conclusions from a comparison of the behavior of two mechanisms as unlike as the most complicated machinery that man's ingenuity has constructed and the mechanics of the human body, but granting this, the fact still remains that mechanical laws are true for both and the effects of stresses, weights, and pressures of various sorts, whether in the body or in the machine, produce effects in obedience to mechanical laws common to both. Wolff's law regarding the principles of trabecular architecture in the structure of bone is an evidence of this. The materials out of which the human body is made and the biologic conditions governing growth and repair add factors which do not have to be reckoned with in the machine when interpreting the effects of faulty mechanical usage, but this constitutes one of the main differences between animate and inanimate mechanisms.

There has been a universal interest manifested in the past few years in visceral ptosis. This has been shared among surgeons, internists, and by some of those interested primarily in the specialties of gynecology, orthopedic surgery, and pediatrics. As a result of the studies evoked by the anatomist it has developed that this condition is widespread; that about one person in every five has some form of this anatomic defect; that though often acquired it is perhaps more frequently congenital, and that its influence upon growth, development, the etiology of various diseases, and general physical vigor or health in its broadest sense is considerable. As is always the case when any new departure is being made there are those whose natural conservatism restrains them from taking any active part in the movement. There are others whose scientific training puts them on the defensive at once; these are those who refuse to accept the suggestive data which have been accumulated by the pioneers in the work as indicating at all that such clues should be followed out. There are also those who swallow the bait and run away to extremes that there is no justification for even in the wildest stretches of the imagination. It remains for

those who first picked up the trail to quietly persist in the search for further confirmation of the truth of their earlier suspicions. This is the present-day situation in regard to visceral ptosis, and the more apparent it becomes that a study of the terminal lesions is not destined to afford much of an explanation of the cause of the disturbances, but that primary, structural, anatomic defects may be looked upon to furnish the reason for the existence of these deformities—for that is what they would be called if we could see them with the naked eye—the more satisfactory are bound to be the results of treatment. The chances of getting at the truth of such a matter as this are hampered because of the fact that we are dependent upon at least two of the above-mentioned types of mind for the accumulation of necessary data. The operating surgeon rarely has the time to make any observations other than those incident to the technique of his operation and the pathology concerned and it is necessary that some one else should make the observation. The representative of the second type knows that it would be unscientific not to investigate, but proceeds to carry on his investigations in a spirit infinitely more reprehensible from the point of view of scientific research, in that he is a prejudiced observer from the start. The greatest harm of all, however, is done by those who without capacity for investigation, and with the commercial, though it may mask under the term scientific, spirit proceed to discover that visceral ptosis is the cause for all bodily ailments and resort to abdominal surgery for their relief.

An intelligent outlook upon the whole question will tend to correct the errors inherent in the point of view of all three different observers. The best corrective for these errors lies in an anatomico-physiologic conception of the situation. This point of view is the one that offers the most in the way of explanation of the factors leading up to the establishment of ptoses. It makes intelligible many of those conditions which seem to be the sequels of these deformities, and it supplies the basis of a rational therapy which is both preventive and corrective. There are among the ptoses two conditions at least; for purposes of description they might be classed as acute and chronic. To the first class belong those cases in which the fundamental anatomic developmental stage has not gone so far as to result in modification of physiologic function, at least to any serious degree. To the second class belong those cases in which the persistence of the anatomic anomaly has resulted in such functional physiologic maladjustments that no mere readjustment of what were the causative, primal anatomic defects is capable of restoring health. Indeed in these cases readjustment of the anatomic defect may no longer be possible.

So much more that is vital is dependent upon the normal function of the intestine than upon the normal function of a joint, or indeed of several joints, that anatomic disarrangements of the

intestinal tube or other of the abdominal viscera intimately related to this functionally must of necessity give rise to more serious disturbance than any disarrangements of anatomic structures in the osseous skeleton. This is, of course, on the assumption that normal anatomic arrangement has something to do with physiologic function. In the case of the skeletal defects such interrelationships have been definitely shown. This gives, *a priori*, ground for the assumption of such interrelationships in the abdominal cavity and opens up a wide field for anatomic and pathologic research as well as for investigation of various problems in the physiologic chemistry of the body. The most obvious disturbance as a result of congenital ptosis of the intestine is the mechanical one, whereby the passage of the food through the intestine is slowed down, and constipation is often the most obvious if not the only unpleasant effect. The secondary disturbances attributable to a sluggish condition of the bowel usually receive but little attention or have but little significance attached to them. An occasional or even an habitual use of catharsis is usually the maximum amount of attention bestowed upon the symptom. Headaches, malaise, offensive breath, anorexia, etc., are taken as a matter of course and ascribed to constipation. Later on as the mechanical difficulties under which the intestinal tube has been operated have increased because of dilatation behind the point of greatest resistance, and because of the other mechanical sequels of the primary maladjustment, the original symptoms are less and less conspicuously mechanical and may become of more serious import. Among the more important of these are the various "kinks" and ileus. Chronic states of ill health, the causes of which are frequently attributed to its most conspicuous symptom, which symptom has to bear the brunt of the therapeutic batteries directed against it, and more often than not successfully withstands the attack. Chronic arthritis may be the form that the fundamental congenital defect brings to the front, or it may be that there are many other of the disease entities which our ignorance of the complexity of interrelations of biologic processes has caused us to establish the practice of referring to these visceral conditions as their cause.

Certain it is that after the mechanical phases of this maladjustment have been in operation for a time that then functional derangement of the gut sets in. It not only fails to move its contents along at a proper rate of speed, but it soon loses apparently some of its value as an absorptive membrane. At the same time the character of its contents becomes altered because of the fact that it has failed in the mechanical part of its function. All the functions of assimilation, so far as they are located in the intestine, become more or less perverted. As the condition becomes more advanced, digestion and body metabolism must be involved also, because one of the most conspicuous gross changes noted in the

intestinal coats in marked cases of this sort is the atony and excessive thinning out of the walls of the intestine. This can scarcely fail, it would seem, to have some effect upon the physiologic activity of such glands as are situated in its walls.

There is reason to suppose that the multitudinous physiologic activities of the body, though they may be able to go on abnormally for some time without any very gross evidences of their maladjustment, must work together in absolute harmony in order that the functions of the organism be continuously at their highest degree of activity and that the efficiency of the individual be kept at its maximum. This state of equilibrium means health.

From what has been suggested by the foregoing it would seem evident that any measures which tend to prevent the establishment of conditions wherein faulty metabolic processes are being put in operation must be employed. In so far as these are dependent upon correctable skeletal defects, benefit will follow the employment of measures directed to the correction of such defects, and in proportion to the capacity for correction will be the benefit to the physiologic disturbance.

I have endeavored to suggest one or two ways in which the skeleton when abnormally set up may unfavorably influence the health. These have been the more obvious and better understood ways. There are many others, apparently the outgrowth of those already suggested. The part played by the ductless glands is more completely beyond knowledge at present possessed than any other physiologic process. How the function of these glands may be influenced by such physiologic disturbances as have already been spoken of it is impossible to say, but it is reasonable to suppose that they may be definitely unsettled in their activities in this manner.

It is easily understood that one of the effects produced by a pronounced visceral ptosis may be exerted upon the circulatory system in the abdominal cavity. The initial effects may be mechanical, but the remote effects may readily be physiologic. The primary disturbance may be an interference with the arterial circulation, restricting blood supply, or upon the venous circulation disturbing the return of blood from the viscera. How such disturbances may affect the functions of such important organs as the spleen and the liver, whose circulation is derived from the celiac axis of the abdominal aorta, can only be surmised. Again, it requires no great stretch of the imagination to see that the lymphatic circulation in the mesentery may be harmfully influenced by conditions of visceral ptosis. The nervous system, though consciously to us only a means of reflecting emotions to our sensoria, enabling us to act in the light of impulses which it conveys, is, nevertheless, of far more importance than such a conception would imply, and has interrelations with the organs of circulation, assimilation, and

digestion which it is highly important should be kept within normal limits in order that the functional activities of the vital organs, so-called, should be capable of being carried out naturally. In childhood and youth such general processes as growth may well be influenced by the train of functional disturbances set in operation by a skeletal anomaly, whether congenital or acquired. This may apply to mental development as well as physical.

These problems comprise much of the work that those who are becoming interested in chronic medicine have lain out for themselves. A new and attractive field for investigation exists. Light is being shed upon many questions which have puzzled all branches of the profession of medicine. The need for a correlation of the knowledge which has been accumulated through the activities of workers in various special lines of research is becoming more and more evident. We are getting past the period when within the narrow limits of our particular spheres of activity we can assume a position of authority and say that this or that ailment can be treated properly only by this or that specialist. It can be properly treated only by the one who has the best conception of the anatomico-physiologic relations of the condition before him, and is broad enough to act on that knowledge. A better conception of the functional anatomic relations of the human being, not merely the ability to recognize and call by name its structural components, is what is necessary in medicine and surgery. When the profession recognizes this and bases its treatment upon such knowledge, some at least of our present-day problems are certain to become easier of solution, and mankind at large will be the gainer.

THE VALUE OF X-RAY EXAMINATIONS IN THE DIAGNOSIS OF ULCER OF THE STOMACH AND DUODENUM.¹

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THE diagnosis of ulcer of the stomach and duodenum is at times a most difficult problem. Not infrequently important symptoms are absent and the cases then become so atypical, that any

¹ Presented at the Meeting of the Association of American Physicians in Washington, May 7, 1913.

additional aid in diagnosis must be looked forward to with great satisfaction. The x -rays have presented us with an important additional means of diagnosis in the study of this affection. While we do not believe that this method is as yet sufficiently well developed to be relied upon alone, yet we are confident that it often offers most valuable assistance as an aid in diagnosis of quite as much practical value, as any of the important symptoms of the disease, and taken in connection with the other signs is of the greatest diagnostic help. We have selected from our 80 cases of peptic ulcers, in which x -ray examinations have been made, 20 for this report, including those only concerning which we could feel confident as to the correctness of the diagnosis. Of these there are 10 cases of duodenal and 10 cases of gastric ulcer. Three of these cases (V, XV, and VIII) were operated on, and the diagnosis was thus confirmed. Three others (XII, XVIII, and XIX) had been operated on, and the ulcers revealed at the time of operation, but were not interfered with, while the remaining 14 presented such typical symptoms of ulcer, including the presence of blood in the stools, that the correctness of the diagnosis in these, too, remains undoubted.

The cases were first studied clinically, and then without any note being given as to the nature of the disorder, were sent for x -ray examinations. The two reports were then placed side by side and the clinical and x -ray diagnoses corresponded so closely in every instance as to make the results appear most striking.

The x -ray diagnosis of gastric ulcer and duodenal ulcer has engaged the attention of the Röntgenologist ever since the production of high-power apparatus has made it possible for us to get practically instantaneous x -rays of the gastro-intestinal tract.

It is, however, only in the last two years that we are really beginning to observe results upon which some reliance may be placed. The old theory that there is a possibility of diagnosing ulcer by bismuth adhering to the raw surfaces is now practically abandoned inasmuch as experience has taught us that this rarely happens because of the fact that the irritability of the raw surface produces hypermotility, with violent contractions, so that it is almost impossible for the bismuth to adhere to the raw surfaces.

At present we are relying more upon the functioning of the stomach and intestines than upon the actual demonstration of the ulcer. Curiously enough, the diagnosis of duodenal ulcer is much simpler than that of gastric ulcer. One can practically always rule out the presence of a duodenal ulcer, but one cannot always rule out the presence of gastric ulcer. The true line of distinction is the fact that in an irritating lesion of the stomach, such as an ulcer, the hypermotility produced by it causes a tonic contraction of the pylorus, with consequent retention of gastric contents, over a

shorter or longer period, according to the situation of the ulcer, and also the deformity that the lesion may produce. On the other hand, in a lesion of the duodenum, we have again a hypermotility not only of the duodenum but of the stomach itself; but in this case we do not have the spastic condition of the pylorus, and consequently the hypermotility produces a rapid emptying of the stomach contents. For example, in our experience in simple ulcer of the duodenum not complicated by adhesions we find the stomach will invariably empty the greater part of its contents in from fifteen to twenty minutes, and will be completely emptied in from forty minutes to an hour. In gastric ulcer we have just the reverse. There will be the primary quick expulsion of contents and then the spastic condition of the pylorus appears, and we have a retention, varying anywhere from two to four hours, depending upon whether the lesion is a simple one or complicated by adhesions.

Let us take up the consideration of the duodenal ulcer. Our experience seems to show that there are certain characteristic features connected with this lesion, which are more or less present in all cases. We have decided hypermotility, yet the contractions are quite uniform, and there is no tendency toward hour-glass formation of the stomach. The pylorus is patulous, and the bismuth flows quite freely into the duodenum. The duodenum is in active contraction, and in many of the uncomplicated cases we find that there is a vacant area in some portion of the duodenum, and this area will persist throughout the period of the examination. At times we may observe bismuth running along either side with the vacant area between the bismuth.

Whereas this has not been proved experimentally, yet we are inclined to believe that this vacant area is the seat of the ulcer, and owing to its raw surface and irregularity the bismuth does not adhere to it; consequently we have this area free, which for want of a better name we have termed "vacant area." In all of the cases we do not have this area free from bismuth, and we are inclined to believe that this fact is dependent entirely upon the condition that the surface of the ulcer presents at the time of the examination. In two of our cases (E. L. R. and J. P.) which have not been included in this report, and in which there had been a fresh hemorrhage within twenty-four hours previous to examination, we have found that it is extremely difficult to observe bismuth in the duodenum; the entire duodenum being in such a state of irritability with consequent hypermotility that the bismuth would be shot through the duodenum almost instantly. Then we have another class of cases with active symptoms where the ulcer was not of long duration, and yet apparently not complicated by adhesions. In these cases the vacant area occurred most frequently (II, III, IV, VIII, XI, XII, XIII, XVII). In the third type of cases in which the ulcer was complicated by the

formation of adhesions, the vacant spot was practically absent. We can account for this by the fact that the adhesions probably lessen the hypermotility of the duodenum, and consequently the bismuth cannot be expelled so quickly from the raw surface. (Cases XII and XIX.)

The first two classes of cases are the most easily diagnosed. Care, however, must be taken not to confuse them with another condition in which we may have a rapid emptying of the stomach, namely, with hypochlorhydria (*achylia gastrica*). In this condition we have a patulous pylorus, so that the stomach contents flows through quickly and freely. This condition, however, is not characterized by the same active contraction as we usually have in the duodenal lesion.

Nothing but the clinical findings would differentiate these two points absolutely. The third type of cases, in which we have an old ulcer complicated by adhesions, is the most difficult to determine. Here the duodenum, and even the stomach, may be so tied up with adhesions as to interfere seriously with the motility of these parts, but even in these cases we find that the stomach is making a determined effort to expel its contents, and shows all the evidences of hypermotility, and at the same time we do not see any bulging of the walls around the pylorus, such as is commonly seen when we have a true obstruction in that region. The duodenum is likely to show constrictions at the seat of the lesion, and if the ulcer is still present we may or may not have a vacant area. The stomach contents as a whole is expelled more quickly than in a normal stomach. In the case of F. H. M., a male, aged sixty-one years, who presented many symptoms of duodenal ulcer, but had no blood in his stools, and who had a marked gastric and duodenal hypermotility, together with the vacant area in the duodenum, an ulcer was not noted at operation, though the duodenum was not opened; however, a band of adhesions was present connecting the duodenum with the gall-bladder.

Our general conclusions in reference to duodenal ulcer are these: There is excessive hypermotility of the stomach, with rapid emptying of contents, so that the greater portion of the stomach contents is emptied within the first half hour, the stomach contraction being practically normal, and there is no evidence of hour-glass formation. There is hypermotility of the duodenum, with formation of a vacant area which remains fixed in all the examinations. The presence of a duodenal ulcer in simple cases uncomplicated by adhesions can practically always be determined.

In gastric ulcer we are dealing with a much more difficult question. Here the question of the normal motility of the stomach is still open to debate, as evidenced by the fact that various authorities have given from two to six hours as being a normal period

for expulsion of the bismuth contents. At present it seems to us that the gastric ulcer can be diagnosticated in certain situations only. From the *x*-ray standpoint we are able to see practically only one surface of the stomach and a portion of the greater and lesser curvatures. Should the ulcer be situated on the posterior surface of the stomach near the lesser curvature, it is not visible because the bismuth contents of the stomach completely obscures that side, consequently we are unable to see any alterations or irregularities of the peristaltic waves. It is only when the lesion is situated on the anterior surface of the stomach, and along the anterior surface of the lesser and greater curvature, that we can come to any conclusion. If the lesion is on the lesser curvature close to the pylorus, by making repeated examinations of the stomach we are able to see irregularities in the peristaltic waves, due to the induration and partial fixation of the ulcer.

If the ulcer happens to be in the profile we might obtain an irregular area not covered with bismuth. Here again we have active contractions with primary rapid expulsion of contents, so that we will almost invariably find the Bishop's cap filled. (We are speaking now, of course, of those ulcers which are not in the pylorus itself, and producing active obstruction.) We get an excessive irritation from the ulcer with a consequent hypermotility, and a spastic condition of the pylorus, so that for the time being there is practically no expulsion of contents. It is only when this spasticity relaxes that a portion of the bismuth is expelled. The act of expulsion, it seems, sets up in waves, and again we have a complete closure of the pylorus, so that the expulsion instead of being regular and rhythmical is decidedly spasmodic and in spurts. When the ulcer is situated just within the pylorus we may have absolute retention over a period of several hours more than normal. And again when the bismuth is expelled it may come in two streams, appearing as if there were some obstruction, with small apertures on either side. In these cases we have found that this vacant area in the pylorus is due to the ulcer, and the excessive irritability has almost diverted the stream to each side of it. In gastric ulcer, whatever its situation, we can always look for retention of contents. Notwithstanding the hypermotility of the stomach, we do not have a hypermotility with expulsion of contents, but, on the contrary, retention.

In these lesions we frequently find a tendency to hour-glass formation, due to spasmodic contraction, with all the stomach contents in both the upper and lower poles. This has never been observed in duodenal ulcer. (Cases I, IV, V, VII, IX, X, XIV, XV, XVI, XX.)

The diagnosis between gastric and duodenal ulcer from clinical signs alone is often very difficult, and many clinicians consider it impossible in many instances to differentiate between the

two. The *x*-ray findings of the two conditions differ, however, so markedly that this method affords an almost positive means of differentiation.

Since we have taken up the positive phase of ulcer it is wise to draw some conclusions as to the negative finding. In the first place we believe that we can rule out positively the presence of a duodenal ulcer. If we observe that the stomach contents are not expelled promptly, and that the greater portion remains after the lapse of an hour, we can maintain confidently that the trouble is not in the duodenum. Even in the old chronic ulcer, with adhesions, the motility is so marked that it cannot be overlooked. The negative diagnosis of gastric ulcer is not so certain. So many complicating phases are present in these cases that the retention of bismuth in the stomach does not appear to have the same significance as the hypermotility in duodenal ulcer. As has been pointed out in gastric ulcer, we have a spastic retention. In simple atony and in prolapse we may have retention, and yet the spastic character of the retention is not present, nor is there any tendency toward the formation of an hour-glass stomach.

Another very important point, which our studies have brought out in connection with duodenal ulcers, is that in a rough way we can approximately determine the degree of healing of the ulcer. In duodenal ulcer, when the patient is given the rest treatment and placed upon the proper diet, all symptoms will gradually disappear, and the patient will become, comparatively speaking, well. This usually takes place in from four to five weeks. At the end of this time, however, if a second bismuth examination be made, we will usually find the same characteristic signs present as in the fresh ulcer, though the patient shows no symptoms whatever. In a series of cases of duodenal ulcer, that have been examined from three to five weeks after the absence of symptoms, we have practically found no change in the motility of the stomach. (Cases II and XVII.) The same hypermotility persists, indicating that there is still an irritating lesion present in the duodenum.

When these patients are given the ordinary diet their symptoms are apt to recur in a short time. If treatment, however, is continued longer our experience has demonstrated that as the ulcer continues to heal the motility of the stomach returns to a more normal condition, and by making repeated observations over a long period of time we can observe by the *x*-ray examinations when the ulcer is healed (Case III). There can be no question but that this is one of the most important findings of this kind of work, inasmuch as until this method was employed there was absolutely no means of determining whether ulcers had healed or not. Our only means of determining this question has been by a return of symptoms, when the patient was placed upon an ordinary diet, and this simply means a relapse for the patient.

By means of x -ray examinations made from time to time we are thus enabled to determine the progress of healing.

CONCLUSIONS. From our studies of the twenty cases of peptic ulcer in which x -ray examinations were made, together with our experience with many other cases, we believe that we are justified in drawing the following conclusions.

1. The x -ray offers most valuable assistance as an aid in the diagnosis of peptic ulcer; and although this method is not yet sufficiently well developed to be relied upon alone without entering into the clinical aspect of the disease, it is of the greatest diagnostic help in obscure cases.

2. In duodenal ulcer there is an excessive hypermotility of the stomach, with rapid evacuation of the contents, so that the greater portion of the gastric contents is emptied within the first half hour; there is hypermotility of the duodenum, with formation, usually, of a vacant area, which remains fixed in all of the examinations.

3. The diagnosis of gastric ulcer can only be made in certain situations: that is, when the lesion is situated on the anterior surface of the stomach, and along the anterior surface of the lesser and greater curvature. We have in this condition an excessive irritation from the ulcer, with a consequent hypermotility, and a spastic condition of the pylorus, so that for the time being there is practically no expulsion of the bismuth. It is only when the spasticity relaxes that a portion of the bismuth is expelled. In gastric ulcer, whatever its situation, we can always look for retention of contents. In certain instances there is a vacant area in the pylorus; there is frequently a tendency to hour-glass formation.

4. The x -ray affords an almost absolute means of differentiating between gastric and duodenal ulcer.

5. By means of the x -ray we can positively rule out the presence of a duodenal ulcer.

6. We can approximately determine the degree of healing of an ulcer which cannot be as certainly determined in any other way.

We append a brief abstract of the histories of our cases.

CASE I.—February 5, 1911. Gastric ulcer. C. G., female, aged sixty-one years. The patient had had symptoms of indigestion for two years, consisting of pain, pressure, and fulness after meals, and nausea but no vomiting. The symptoms were more marked after solid than with liquid foods; they had become more and more intense, until the patient vomited large amounts of the undigested food; she had lost but a small amount of flesh, and the discomfort after meals had gradually become more aggravated. On examination peristaltic movements were visible, and an extremely painful area in the epigastrium presented itself. There was no palpable mass in the abdomen; the gastric contents showed a total acidity of 40; free hydrochloric acid was absent. There

was an absence of lactic acid and the Oppler-Boas bacilli; blood was, however, present. A retention meal was given at night, and the stomach washed the following morning, when a large quantity of the food remains was returned. Occult blood was observed in the stools. A diagnosis of gastric ulcer with obstruction was made (notwithstanding the absence of free hydrochloric acid), because of the character of pain after meals, the duration of the disease, and the slight loss of flesh.

An x-ray examination revealed a stomach situated high up, with an extremely bulbous pylorus, and definite retention due to obstruction was noted. The patient was operated on April 3 by Dr. J. M. T. Finney. A thickened pylorus with obstruction was revealed, together with multiple ulcers in this region. A pylorotomy was performed and the patient made an uneventful recovery from the operation.

CASE II.—December 2, 1902. Duodenal ulcer. W. T., male, aged forty-seven years. The patient had had indigestion for several years, with periods of complete remission, lasting several weeks to a month. The indigestion consisted of pain in the epigastrium two hours after meals, which was relieved by food, as well as when in the recumbent position. This discomfort was less with liquids than with solid food. On examination an epigastric painful point was revealed. No other tender areas were observed. The gastric secretion presented a total acidity of 60; free hydrochloric acid, 60. Occult blood was present in the stools.

An x-ray examination presented an extreme gastric hypermotility, with rapid expulsion, the stomach being completely empty in an hour and a half. In the duodenum there was a small vacant area, at which bismuth was found absent, though there was bismuth in front of it and behind it ("vacant area").

CASE III.—November 26, 1912. Duodenal ulcer. C. F. B., male, aged sixty-one years. This patient had had numerous attacks of gastric pains extending over periods of from two to three months for the past ten or twelve years. These pains would appear two hours after meals, and would be temporarily relieved by food and by alkalies, and would also disappear when the patient was in the recumbent position. Tarry stools were present in one attack. The last attack had been present for about two months. The patient had lost eight to ten pounds in weight. A gastric analysis, made during a former attack (four years before), revealed a total acidity of 96; free hydrochloric acid, 78; occult blood was present in the stools.

An x-ray examination showed an extreme hypermotility of the stomach, with an area in the duodenum uncovered with bismuth ("vacant area"). On March 31, 1913, another x-ray examination was made. Hypermotility was present, but not to the same degree as in the previous examination. This would indicate that the

ulcer was going on to a healing stage. It was not so active as in the previous examination.

CASE IV.—December 27, 1912. Gastric ulcer. J. S., female, aged thirty years. Patient had been suffering acutely for the past three weeks with marked epigastric pain, passing into the back between the shoulder-blades. The pain was most acute immediately after taking food, and much more so after solid than liquid food. She was relieved when in the recumbent position. There was frequently nausea and occasionally vomiting. The patient had vomited small quantities of blood. The gastric contents presented a total acidity of 54; free hydrochloric acid, 48; blood; a bit of necrotic tissue; occult blood was present in the feces.

An *x*-ray examination showed a somewhat bulbous pylorus, which at times appeared in a state of extreme tonic contraction, the bismuth, however, going through very rapidly. From the state of tonic contraction and bulging of the stomach there must have been some inflammatory condition within the stomach just at the pyloric ring.

CASE V.—September 20, 1912. Gastric ulcer. S. M. B., male, aged fifty-six years. (Case referred by Dr. Boyd, of Jacksonville, Florida.) The patient had been affected for a number of years with gastric disturbances, with remissions for variable periods of time (from two weeks to a month). The attacks were characterized by pain coming on a short time after meals, *i. e.*, in from fifteen to thirty minutes; they were accompanied by nausea and occasionally by vomiting. Eructations of gas and acid eructations were frequent. The distress was increased on taking solid food, and was less on liquids; it was also lessened when the patient was in the recumbent position. On examination an epigastric painful area was manifested. The gastric contents presented a total acidity of 74; free hydrochloric acid, 0.21 per cent.; occult blood was present in the stools.

An *x*-ray examination revealed a persistent absence of bismuth about the junction of the duodenum and pylorus (vacant spot), the motility of the stomach being markedly increased. Dr. Boyd operated on the patient on December 1, 1912, and found a pyloric ulcer evidently of long standing, and there was marked induration and quite a puckered condition of the stomach wall at this site.

CASE VI.—May 21, 1912. Duodenal ulcer. D. S., male, aged thirty years. The patient had had three distinct attacks of gastric disturbances of the same character. The first attack occurred three years before, the second attack a year later, and the present attack began a few weeks ago. Between the attacks the patient was perfectly well, and could partake of all kinds of food. The attacks began with heart-burn, pressure, and an uncomfortable sensation in the region of the stomach, which was soon followed

by pain; the pain appeared several hours after meals, and was relieved by food; the pain was usually relieved when the patient was in the recumbent position, as well as by alkalies. The pain appeared frequently at night, awakened the patient, but lasted only for a short time. On examination the patient presented a painful epigastric area. The gastric secretion showed a total acidity of 80; free hydrochloric acid, 0.21 per cent. There was occult blood in the stools.

An x-ray examination showed a marked gastric hypermotility, seven-eighths of the bismuth having been expelled from the stomach in forty-five minutes; there was also an area in the duodenum just in front of the pylorus, where no bismuth remained. In none of the plates would any bismuth adhere to this small rounded area, which was about the size of a 5 cent piece, bismuth appearing on both sides of it ("vacant area"): there was in addition a decided hypermotility of that portion of the duodenum, bismuth passing through that area with unusual rapidity. With this hypermotility and with the vacant area in the duodenum the diagnosis of duodenal ulcer was confirmed. There was in addition a much dilated cecum, prolapse of the ascending and transverse colon, and all were firmly bound down to the cecum.

CASE VII.—December 20, 1912. Gastric ulcer. J. W. P., female, aged forty-seven years. This patient was first affected with the digestive disturbance two years before; at that time she complained of pain appearing two to four hours after meals, heartburn, and acid eructations. The pain was relieved by the taking of food and by alkalies. There was no difference as to the production of the pain, in relation to the food, solid food causing as much pain as liquids. The pain always disappeared, however, in the recumbent position. An examination at that time revealed an epigastric painful area; a gastric contents with a total acidity of 100; free hydrochloric acid, 54; occult blood was present in the stools. A diagnosis of duodenal ulcer was made and a Leube rest cure undertaken; the patient recovered entirely in the course of six weeks, and was able to partake of all foods without discomfort. On December 20, 1912, she again presented herself for treatment. For the past four weeks she again complained of gastric pain, appearing fifteen or thirty minutes after meals, with distress from gas, some eructations, nausea, vomiting of an acid secretion, and at times a brownish matter; great relief was experienced from vomiting as well as when the patient was in the recumbent position. An examination revealed an epigastric and dorsal painful area; a gastric contents with a total acidity of 84; free hydrochloric acid, 0.22 per cent.; and blood; tarry stools were likewise observed. There was no evidence of peristaltic movements, and after a retention meal given at night the stomach was found perfectly empty the following morning.

An x-ray examination revealed a long vertical stomach, the greater curvature lying well below the crest of the ilium. Active motility was present, but the pylorus was very irregular in shape, and the stomach around the pylorus was bulged out, showing definitely that there was some obstructive condition at the pylorus itself. Notwithstanding the active motility of the stomach a good portion of the bismuth was still left in the stomach at the end of two hours. The delay in expulsion was due to a great deal more than the extreme prolapse, and was in all probability due to an ulcer.

CASE VIII.—January 11, 1913. Duodenal ulcer. C. G., male, aged thirty-four years. This patient had had attacks of indigestion for the past four years, lasting from two or three weeks to three or four months at a time. The attacks were all characterized by similar symptoms. He had been affected with the present attack for the past four months. The symptoms complained of consisted of pains in the region of the stomach, appearing four or five hours after meals, which were intense at times, and which were relieved by the ingestion of food and also by soda bicarbonate. The patient was extremely constipated and had lost fifteen pounds in weight. He complained of the acid eructations, but was not nauseated, and did not vomit. An examination of the patient revealed a painful area to the right of the median line. The gastric contents showed a total acidity of 88; free hydrochloric acid, 0.21 per cent.; occult blood was present in the stools.

An x-ray examination presented the stomach in a state of excessive hypermotility, with rapid expulsion of the bismuth contents into the duodenum. Just outside of the pylorus and in the first portion of the duodenum there was a ragged area in which no bismuth was found ("vacant area"). This persisted in several plates, and from this, together with the hypermotility of the stomach, we could say confidently that there was an ulcer in the duodenum causing this change.

CASE IX.—January 8, 1913. Gastric ulcer. J. G., female, aged fifty years. The patient had been affected with the present condition for the past two years; at times entire relief was obtained for a period of from two or three weeks. The symptoms complained of were a burning sensation in the region of the stomach, pain soon after the ingestion of food, followed by nausea and frequently by vomiting. The pain was so increased on taking solid food that the patient had almost entirely discontinued solids, and was living on liquids. The quantities vomited were usually small in amount, and there had never been any evidence of food taken the day before in the vomitus. The symptoms had been markedly lessened since she had been on liquid diet; the patient found great relief when in the recumbent position. An examination of the abdomen revealed an epigastric painful area, exquisitely painful

to pressure. The gastric contents presented a total acidity of 70; free hydrochloric acid, 62; occult blood was present in the stools.

An x-ray examination presented a large stomach, the pylorus drawn well over to the right side, and lying rather high up. The motility of the stomach was good, but the expulsion was poor, indicating the presence of some inflammatory condition in the stomach, causing retention. On account of the abnormal position of the stomach well over to the right side one had to take into consideration adhesions, but from the position of the stomach and the way it was functioning we believe that we had an inflammatory condition of the pylorus in the form of an ulcer, producing retention, with adhesions outside, holding the stomach in an abnormal position.

CASE X.—January 7, 1913. Gastric ulcer. C. R., male, aged twenty-five years. The patient had been affected with indigestion for the past three months. His complaints consisted of pain fifteen to thirty minutes after eating, followed by nausea and vomiting. His pain was entirely relieved by vomiting. He had much less difficulty with liquid food than with solids; he was much annoyed by heart-burn, acid eructations, and gas, and was markedly constipated. During the past three months he had frequently observed tarry stools. On examination a tender epigastric area was revealed which was exquisitely tender to pressure. His gastric contents presented a total acidity of 56; free hydrochloric acid, 42. A retention meal given at night revealed the stomach empty when followed by lavage the next morning. There was occult blood in the stools. An x-ray examination presented a prolapsed and enlarged stomach, yet notwithstanding this the organ appeared actively motile. Bismuth was expelled with some difficulty, so that there was some retention at the end of three hours. In all of the plates there was an irregular area, to which bismuth did not adhere, just inside the pylorus at the lesser curvature of the stomach.

We were here dealing with a gastric ulcer situated at the lesser curvature just within the pylorus.

CASE XI.—January 18, 1913. Duodenal ulcer. A. W. M., male, aged twenty-three years. The patient had had disturbances with his digestion for the past year. He had pain in his stomach two hours after meals, which was temporarily relieved by food as well as when he was in a recumbent position. He had less distress from liquids than from solid foods. The pain was distressing at times, but could always be relieved by the ingestion of food; even the drinking of hot water relieved it. The patient had not had nausea or vomiting, but was constipated; was nervous and suffered with headaches. On examination an epigstric painful area was revealed, also a painful area in the back to the left of the spine at the level of the tenth dorsal vertebra. The gastric contents pre-

sented a total acidity of 85; free hydrochloric acid, 0.22 per cent.; and blood. The stools showed occult blood.

An x-ray examination revealed a marked gastric hypermotility with an irregular area in the duodenum, not coated with bismuth, and which persisted in all the plates ("vacant area").

CASE XII.—January 25, 1913. Duodenal ulcer. J. H. D., male, aged thirty-nine years. The patient was operated on in May, 1912, for cholelithiasis; no gallstones were found, but a chronically inflamed appendix was removed. At this time the surgeon noted the presence of a partially healed duodenal ulcer. The patient recovered from the operation, and after three weeks was taken with his present disorder. The symptoms manifested were nausea, fainting attacks, and severe epigastric pains, which lasted for a period of from ten days to two weeks, and would disappear for from one to four weeks, and then recur. The pain appeared two or three hours after meals, and was relieved by food and by the use of soda. On examination an epigastric painful area was revealed. The gastric contents presented a total acidity of 72 and free hydrochloric acid of 62. A retention meal given at night showed the stomach completely empty of food remains the following morning. Occult blood was present in the stools.

An x-ray examination showed a long tubular stomach prolapsed, the pyloric end lying well over to the right side. There was a hypermotility of the stomach and duodenum and a vacant area in the duodenum. There were in addition adhesions around the region of the appendix involving the cecum, ascending and transverse colon, and the sigmoid. These produced sluggish motility, but there was no evidence of obstruction.

CASE XIII.—January 2, 1913. Duodenal ulcer. M. S., female, aged sixty-five years. The patient had had indigestion off and on for four years; she was taken acutely ill with what was termed an ulcerated stomach, and vomited a large quantity of blood at that time. The present attack dated back one year. It was characterized by severe pain appearing two hours after eating, accompanied at times by nausea and occasionally by vomiting. Liquids seemed to give less distress than solids. The pain was relieved by the ingestion of food, by the use of alkalies, and by the patient assuming the recumbent position. Eructations were present to a marked degree, and heartburn was quite frequent. Tarry stools had frequently been observed. On examination an epigastric painful area, exquisitely tender to pressure, was revealed, as well as a dorsal painful area to the left of the spinal column and at the level of the tenth dorsal vertebra. The gastric contents showed a total acidity of 75; free hydrochloric acid, 0.19 per cent.; occult blood was present in the stools.

The x-ray examination showed that practically all the abdominal organs were displaced, the position being very abnormal, due to

Pott's disease, which was marked. There was, however, extreme hypermotility of the stomach, so that three-fourths of the contents were emptied in from five to twenty minutes, and in one hour and ten minutes the stomach was completely empty; one portion of the duodenum was rather bulbous, and just behind this bulbous position was an area free of bismuth ("vacant area"). This persisted in several plates, so that there was evidence that we had here an ulcer of the duodenum. The abnormal position of the duodenum and the stomach was entirely due to the Pott's disease and not to adhesions.

CASE XIV.—December 25, 1912. Pyloric ulcer. J. B., male, aged thirty-six years. The patient had had stomach disturbances for four years, with periods of freedom from distress lasting several months. The present attack dated back one month. It was characterized, as all of the former attacks had been, by the following symptoms: intense pain appearing soon after meals; less pain, however, from liquids than solids; the pain disappeared when the patient was in the recumbent position; at times there was nausea and occasionally vomiting, with marked relief of pain after vomiting. The patient suffered from acid eructations and heart-burn; he had never vomited blood. On examination a marked epigastric painful area was revealed. The gastric secretions showed a total acidity of 88; free hydrochloric acid, 22. On lavage of the stomach in the morning, following a retention meal given at night, the stomach was found completely empty of all food remains. Occult blood was present in the stools.

An x-ray examination revealed a cow-horn stomach and a rather bulbous pylorus, the motility of the stomach being good, but the expulsion of the contents was slow. Just above the pylorus a number of plates showed an irregular ragged area, with practically no bismuth adherent "vacant area." This case was clearly one of ulcer at the pylorus.

CASE XV.—January 1, 1913. Gastric ulcer. L. K., male, aged thirty-nine years. The patient had a stomach disorder similar to the present attack a number of years previously. He again complained during the past three months, though he had had periods of relief of short duration. He suffered with severe pain, usually about three hours after meals, though this was not constant, as many times the pain appeared immediately after meals; nausea and vomiting were irregularly present, and pain was relieved after vomiting. There were acid eructations, but alkalies did not relieve the pains. The patient had less distress on liquid food, and was usually relieved when in the recumbent position. On examination a painful epigastric area was revealed, and no peristaltic movements were observed. The gastric contents presented a total acidity of 58; free hydrochloric acid, 38. Food remains and blood were observed in the gastric contents on lavage of the stomach

in the morning, a retention meal having been given the previous night.

An α -ray examination revealed a long prolapsed stomach, with a sawed-off pylorus, that is, no evidence of any pylorus could be made out. The pylorus was, however, not completely obstructed, as there was some expulsion of contents, though there was a great deal of retention, with consequent dilatation of the stomach. Contractions of the stomach were quite active, however, showing that the dilatation was not primary, but was evidently secondary to some obstruction of the pylorus. This obstruction was more from within, and was probably due to an old ulcer, with the formation of a great deal of scar tissue and contraction.

On January 16, 1913, the patient was operated on by Dr. J. M. T. Finney. An ulcer was found near the pylorus in the lesser curvature of the stomach; this ulcer was resected and a pyloroplasty performed.

CASE XVI.—January 2, 1913. Gastric ulcer. B. D. C., male, aged thirty years. The patient had been affected with indigestion for five years, with periods of remission. Five years previously he was operated on for appendicitis for symptoms much the same as at the present time. Four years before his symptoms became much more aggravated while training at Muldoon's. The symptoms finally abated after several months. Several attacks followed. The last attack began November 15, 1912, and the patient had been troubled ever since. He had pain beginning in the epigastrium, and radiating toward the back, following soon after the ingestion of food; more so after solids than after liquids, and was usually relieved by the recumbent position, though at times the pains were severe at night. Eructations were present, which were sometimes acid in character; there was nausea at times, but no vomiting. On examination an epigastric painful area was revealed. There was also a dorsal painful area in the back, to the left of the spine, at the level of the tenth dorsal vertebra. Slight peristaltic movements were visible. The gastric contents presented a total acidity of 72; free hydrochloric acid, 0.19 per cent. There was occult blood in the stools. A small amount of food remains was obtained in the wash water the morning following a retention meal given at night.

An α -ray examination showed a large stomach, the pyloric end being drawn well over to the right side, and apparently fixed in that position. The motility of the stomach was quite good, but notwithstanding this, at the end of two hours and a half, a great quantity of bismuth remained in the stomach. It appeared evident that we were dealing with some true pyloric obstruction, as one cannot conceive of the shape of the pylorus and its position due to adhesions causing such complete obstruction, and consequently

must assume that there was some inflammatory condition within the stomach, an ulcer, leading to this abnormality.

CASE XVII.—January 2, 1913. Duodenal ulcer. D. G. K., male, aged fifty-one years. This patient had had an acid dyspepsia for years; he had been troubled with gas and with regurgitation of acid food. In May, 1912, he had some pain in his stomach, which appeared three hours after meals, and which was relieved by food and by the use of soda. On this account he was forced to diet himself, and had to abstain from all indigestible foods. The pain continued and he finally vomited a large quantity of blood. This was soon followed by the passage of tarry stools. An ulcer rest cure was undertaken, and the patient made a speedy recovery.

January 2, 1913. His pains had nearly, though not entirely, disappeared; heart-burn was still present, and there were eructations of acid material. A very slight epigastric tender area still persisted. The gastric secretion showed a total acidity of 72; free hydrochloric acid, 58. Occult blood was present in the stools.

An x-ray examination revealed a hypermotility of the stomach, as over three-fourths of the contents were expelled within three-quarters of an hour. In the first portion of the duodenum there was a small constricted area ("vacant spot") and beyond that point a slight bulging. With this condition it was evident that there was some inflammatory lesion of the duodenum in the form of an ulcer.

CASE XVIII.—November 4, 1913. Duodenal ulcer. M. L., male, aged thirty-four years. The patient had had slight digestive disturbance for some time prior to October 23, 1912, on which day he was suddenly taken with a violent attack of pain in the abdomen and was removed to a hospital, the abdomen opened, and a perforating duodenal ulcer was revealed; a rapid life-saving operation was performed, but the ulcer was not excised; three or four weeks later, when the patient was placed on nearly full diet, he was taken with pain, which began two or three hours after meals, and which was relieved by food. The pain has continued to the present time; he has in addition heart-burn, and, at times, acid eructations. On examination an epigastric tender point was revealed, as well as a tender area in the back to the left of the spine, on a level with the twelfth dorsal vertebra. The gastric secretion presented a total acidity of 86; free hydrochloric acid, 0.21 per cent.; the stools contained occult blood.

The x-ray examination revealed a long-drawn-out stomach, with the pylorus to the right side, rather bulbous in character, with some obstruction at that region, with excessive hypermotility. These two facts were apparently contradictory, indicating that we were dealing with two conditions: adhesions involving the pylorus from an old operation, and a duodenal ulcer.

CASE XIX.—February 11, 1912. Duodenal ulcer. M. B., male, aged thirty-nine years. The digestive disturbance began in this patient in 1901, when he began to complain of severe pain two to four hours after meals, together with acid eructations, gas, and and frequently of vomiting. The vomited matter consisted mainly of food, and was frequently bloody; the bowels were constipated, and often of a tarry appearance; alkalies relieved his symptoms temporarily, and relief was always afforded by the ingestion of food. Periods of relative comfort alternated with numerous attacks of the kind already described. Five years previously the patient had a sudden and violent attack of pain, and was operated on for a perforating duodenal ulcer; this was followed by a diffuse peritonitis; then double empyema, and four months later obstructive symptoms manifested themselves and a posterior gastro-enterostomy was performed; the ulcer was observed covered over by some scar tissue, and surrounded by many adhesions. The patient was relieved, and was again operated on a little later for an incisional hernia, and the appendix was removed. For several weeks the patient had been suffering with a recurrence of his former symptoms, pain appearing two or three hours after meals, which was relieved by food or by lavage. There were acid eructations, but nausea and vomiting were absent. On examination a slight epigastric painful area was revealed. The gastric secretion presented a total acidity of 71; free hydrochloric acid, 62; occult blood was present in the stools.

An x-ray examination revealed the gastro-enterostomy opening free and patent; there were adhesions around the pylorus and duodenum, with increased motility of the duodenum.

CASE XX.—February 27, 1913. Gastric ulcer. M. A., female, aged thirty years. The patient had complained of stomach trouble for fifteen years, with periods of rather severe gastric pain; she suffered with nausea, but only rarely with vomiting. The pain appeared after eating, and was greater with solid than with liquid food, and was relieved when the patient was in the recumbent position. The gastric secretion showed a total acidity of 70; free hydrochloric acid, 0.42 per cent. The examination of the stools presented occult blood. On examination an epigastric painful area was observed.

An x-ray examination of the stomach revealed a prolapse. The stomach was of the fish-hook type. There was a delay in the expulsion of the stomach contents, which can be easily accounted for by the prolapse; but, on the other hand, there was an eroded area ("vacant spot"), just at the lesser curvature, within the pylorus, which persisted in all of the plates.

THE PRESENT SITUATION IN SYPHILIS.

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ONE great discovery has followed another in syphilis in the last ten years in a way that is without parallel in the history of any other disease.

First there was the demonstration by Metchnikoff and Roux in 1903 that syphilis could be produced by inoculation in chimpanzees, which was soon followed by the discovery that other apes, the rabbit, the guinea-pig, and a few other animals were susceptible to inoculation. Quick upon the heels of this basic discovery, which furnished the first opportunity for experimental study of syphilis, came the discoveries that have so greatly increased our exact knowledge of the disease.

In 1905 Schaudinn and Hoffmann ended the long search for the organism of syphilis by the discovery of the *Spirochæta pallida*.

At almost the same time, in 1905-6, Wassermann, Neisser, and Bruck applied the serum-complement reaction of Bordet and Gengou to the diagnosis of syphilis.

Finally, there has been the development of the arsenical chemotherapy of syphilis, begun by Uhlenhuth, and carried forward so amazingly by Ehrlich by the introduction of salvarsan in 1909.

These fundamental discoveries constitute, of course, an epoch in the history of syphilis, and it is inevitable that they should have produced a complete recasting of the methods of its management. They have in fact revolutionized not only the methods but the principles of its management, and it is to these changes in the practical management of the disease that I would direct brief critical consideration.

The great additions which have been made to the management of syphilis are:

1. Diagnosis by demonstration of the *Spirochæta pallida*.
2. Diagnosis by the Wassermann reaction.
3. The use of the Wassermann reaction as a criterion of the effect of treatment.
4. Diagnosis by Noguchi's cutaneous reaction.
5. Prophylaxis by inunction of 33 per cent. calomel ointment within a few hours after infection.
6. Treatment by salvarsan and its derivatives.

THE DIAGNOSIS OF SYPHILIS BY DEMONSTRATION OF THE SPIROCHÆTA PALLIDA. The presence of *Spirochætæ pallidæ* is the first definite proof of syphilis that can be demonstrated. They are abundant and easily demonstrable at the first appearance of

the initial lesion: before the Wassermann is positive, and before there is any characteristic adenopathy or any eruption. They become less abundant as the chancre ages and somewhat less easy of demonstration, but my experience agrees with that of many others that they can be demonstrated in practically every untreated unhealed chancre. This is not the case if the lesions have been treated, for antiseptic applications, particularly mercurial applications, greatly increase the difficulty of or prevent their demonstration.

As everyone is agreed on the importance of as early a diagnosis of syphilis as possible the serious question at once arises, How distinctive are the characteristics of the *Sp. pallida*, and how much reliance can be placed upon the diagnosis of syphilis solely upon its demonstration? Certain spirochetes resemble more or less closely the *Sp. pallida*, *Sp. refringens*, and *Sp. balanitidis* found in chancres and mucous patches; *Sp. buccalis* and *Sp. dentium* in the mouth; *Sp. pseudopallida* in cancerous ulcers, and the *Sp. pertenuis* of yaws. The spirochetes most resembling *Sp. pallida* are *Sp. dentium* in carious teeth, *Sp. pseudopallida*, and *Sp. pertenuis*.

Most workers of experience believe that the *Sp. pallida* can be definitely distinguished from these organisms, and with that my experience agrees. But it must be emphasized that a reliable recognition of the *Sp. pallida* under dark field illumination or in stained specimens requires a practised careful observer who is habitually doing this particular work. Under these conditions the diagnosis of syphilis by the demonstration of *Sp. pallidæ* can, I believe, be reliably established. In so important a situation as the determination of syphilis in the first days of a chancre, from the recognition of *Sp. pallidæ* alone, I believe it is desirable to determine the character of the spirochetes by two independent observers, in order, so far as possible, to eliminate the personal equation. This I have done in numerous instances, and I have not had disagreement in the decisions.

I do not know of the unreliable work in the diagnosis of syphilis from the spirochetes as I do from the Wassermann reaction—due, I believe, to the fact that the demonstration of the organism is not commonly relied upon for diagnosis—but this is a method of diagnosis easily open to error and abuse. I do not believe the ordinary laboratory man who is not familiar by constant observation with the various spirochetes can be safely relied upon to differentiate the *Sp. pallida* in critical situations. The demonstration of spirochetes under dark field illumination is one of the simplest laboratory procedures, but the reliable differentiation of the *Sp. pallida* is not simply a matter of laboratory technique.

The demonstration of *Sp. pallidæ* in secondary lesions when other evidence of syphilis exists is a less critical matter. Here

the demonstration is only confirmatory evidence, and it has the value of one fact in establishing the diagnosis. Occasionally this is an important fact in determining the character of confusing lesions, particularly on mucous surfaces or at mucocutaneous junctures, occurring in the course of active syphilis.

Unfortunately for diagnostic purposes the spirochetes are so few and so difficult to demonstrate in late (gummatous) lesions that their demonstration is not a practical method for establishing the character of these lesions.

THE WASSERMANN REACTION IN DIAGNOSIS. On the question of the specificity and reliability of the Wassermann reaction there is no need to waste space. The world is agreed in the affirmative upon these points. With the exception of a few now well-recognized conditions, which fortunately are not likely to lead often to confusion with syphilis, the Wassermann reaction is specific for syphilis, and can be elicited in most cases in which the disease is present. It becomes positive only when the disease has become generalized; the reaction is present, therefore, only in about 40 per cent. of cases at the appearance of the initial lesion. During the three weeks after the appearance of the initial lesion it becomes positive in about 75 per cent. of the cases, and when the cutaneous manifestations of the disease become well established, it is positive in practically all untreated cases. In late syphilis the reaction is positive in about 80 per cent. of cases. In latent cases it is positive in about 50 per cent.

In spite of the remarkable trustworthiness of the Wassermann, syphilographers generally, I believe, are conscious of many serious mistakes which are occurring in the practical application of it in diagnosis. These mistakes arrange themselves in three groups:

1. The diagnosis of syphilis from supposedly positive Wassermann's in the absence of syphilis.

2. The failure to recognize syphilis because of a negative Wassermann.

3. The reliance upon the Wassermann in conditions in which the presence or absence of syphilis has no practical bearing upon the lesion under consideration.

1. A positive finding in the absence of syphilis, of course, should not occur with a trustworthy reaction. The fact remains, however, that the mistake of reporting a positive Wassermann, when actually it does not exist and in the absence of syphilis, does occur, and, I believe, not infrequently. I have had this occur more than once in my experience in cases in which the lesions under consideration were not syphilitic, and in which Wassermann's made in my laboratory and, as a control, independently by another reliable worker, were negative.

How can such mistakes occur? Simply from the fact that the Wassermann reaction—absolutely trustworthy in itself, when posi-

tive, if correctly made and correctly interpreted—is done by human hands, and human hands are fallible. Let a laboratory man speak upon this point: “One need not emphasize the fact that in the laboratory there are no infallible methods, a fact which is most glaringly true of the Wassermann reaction. I make this statement taking for granted that the worker is experienced” (Kaplan); and then he recites for illustration a case in which from one serum three reports were obtained: a positive from a tyro; no decision from the second; negative from the third. Again: “In the Wassermann reaction the stumbling blocks are many and can be overcome by experience and practice only. The beginner makes many non-luetic sera positive, the theoretical worker does the same to a lesser extent, and the mature worker fails to report many syphilitic sera as positive.”

The Wassermann reaction has many factors in it to give rise to error, and a reliable Wassermann, therefore, requires experience, careful attention to technique and to controls, and care in interpretation of results. With such requirements it is not surprising that errors occur with careless or immature workers. This is true of the original Wassermann; it is much more true, as nearly all workers are agreed, if the simplified modifications of the Wassermann are used.

2. Inaccurate work may be responsible for some negative Wassermans in the presence of syphilitic lesions, but this mistake of reporting the Wassermann negative when it is actually positive has not been brought to my attention in the way the grosser opposite error has.

Without error in the reaction a negative Wassermann is not rare in late (tertiary) active syphilis; it occurs in 20 to 30 per cent. of the cases. Even in cases of treated active secondary syphilis one sometimes gets a negative Wassermann. It follows therefore that to rely on the Wassermann alone to make a diagnosis of syphilis is to court trouble, and this is the mistake that is constantly being made. It is not a rare experience to see a frank syphilide in the skin left unrecognized and untreated, as far as efficient treatment is concerned, because the Wassermann is negative. And if this occurs with cutaneous lesions of syphilis it surely occurs with internal lesions.

3. The third error, relying on the Wassermann in conditions which have nothing to do with syphilis, we in dermatology occasionally see. In epithelioma, especially epithelioma of the tongue, in lupus, in sycosis, in chronic eczemas of the hands, in various sorts of generalized eruptions, which surely had nothing to do with syphilis—scabies, for example—it has been my experience to see much useless puttering over Wassermans, and in some cases, which happened actually to have syphilis, much mental perturbation because non-syphilitic lesions had not yielded to syphilitic

treatment. The syphilitic, of course, is not immune to other dermatoses; he is actually predisposed to some non-syphilitic lesions, as epithelioma of the tongue; and when one goes to giving weight to the Wassermann in non-syphilitic dermatoses in syphilitic subjects he is soon hopelessly confused.

The deduction to be made from these errors is that we should not neglect other forms of evidence. That unfortunately is the tendency whenever any laboratory test becomes available in diagnosis. I suspect there are few men, with the exception of thoroughly mature laboratory men themselves, who have not a little superstitious super-regard for laboratory findings as compared with clinical observations, when as a real fact they are more open to error and more in need of the qualities of experience and maturity of judgment than are clinical observations.

Nothing is surely more true than that the Wassermann in diagnosis must constantly be checked and compared with the clinical findings. If these are neglected, reliance upon the Wassermann must inevitably involve one in serious mistakes. As a matter of fact the lesions of syphilis upon the surface and at the orifices of the body are, as a rule, perfectly characteristic regardless of the Wassermann; and if these characteristics are neglected or not known the observer who depends upon the Wassermann will overlook one case in every five of them.

In considering the pitfalls of the Wassermann as it is practically applied no suspicion arises as to the real value of that reaction. Carried out with skill and care, and interpreted with appreciation of its limitations, a vast accumulation of experience has demonstrated it to be a perfectly trustworthy test. But it is only one fact, and its value is nearly always as confirmatory evidence of syphilis, of which there is usually abundant clinical evidence also to be found if sought with reasonable intelligence and care. It is the rarest experience to have nothing to indicate syphilis except the Wassermann, and when one hangs a diagnosis of syphilis on that evidence alone he should remember his diagnosis hangs upon a single thread of whose strength he should be perfectly certain. And even when he is certain of his positive Wassermann, if he does not know or consider his clinical conditions, the patient's trouble may still be a pus infection, or tuberculosis, or the itch, or some other non-luetic disease. The Wassermann is not a satisfactory substitute for clinical knowledge.

THE WASSERMANN AS AN INDEX OF TREATMENT. Following the great authority of Neisser, the Wassermann is being widely used as an index of the efficacy and of the necessity for treatment. Neisser's position is this: A positive Wassermann is proof of active syphilis and of the presence of living spirochetes; therefore, a positive Wassermann is an indication for specific treatment. As a corollary of this the efficacy of treatment may be judged

by the effect upon the Wassermann. "Conversely a negative reaction, which means the restoration of the serum to its normal state, signifies generally if not complete destruction of the parasites at least the establishment of a condition of equilibrium between the host and the spirochetes, so that the latter assume the character of harmless saprophytes. If any treatment short of complete sterilization is to be of value it must maintain this relationship; hence the Wassermann reaction should be used to control the treatment, as it is usually the most subtle indicator of a disturbance of equilibrium with a tendency to the assumption of pathogenic activity on the part of the spirochetes." This quotation from Browning and McKenzie states well the position of those who make the Wassermann the basis for the so-called "biologic" treatment of syphilis.

It is not established beyond any possible doubt that a positive Wassermann means active syphilis. This is, however, probably true. All that can with scientific accuracy be said of a positive Wassermann is that it is evidence that the patient has had syphilis—the rest is, in part at least, assumption.

Conversely it is not established that a negative Wassermann means "the establishment of a condition of equilibrium between the host and the spirochetes, so that the latter assume the character of harmless saprophytes." On the contrary, clinical evidence proves beyond doubt that at times with a negative Wassermann the spirochetes may possess their usual virulence. All experience has shown that in 20 per cent. to 30 per cent. of cases of late active syphilis the spirochetes are showing every evidence of pathogenic activity in spite of negative Wassermann. One may even see, as I have seen, mucous patches teeming with *Sp. pallidæ* in late secondary syphilis with the Wassermann negative. So it is not true beyond any possible question that a positive Wassermann means active syphilis, and it is certainly not true that a negative Wassermann means a condition of equilibrium between the spirochetes and the tissues, so that the spirochetes have become harmless saprophytes.

It can be said, however, that the Wassermann reaction in syphilis is not a true specific antibody-antigen reaction. It is established that a specific syphilitic antigen is not necessary to the reaction, and a consideration of all the facts indicates that it is highly probable that the substance in the syphilitic serum that produces the specific Wassermann reaction is not true syphilitic antibody but some undetermined substance. This latter fact is exceedingly important in its practical bearing upon the question of the value of the Wassermann reaction as an index of treatment. For if it were true that the Wassermann reaction is an index of the amount of antibodies produced—in other words, of the immunity which the individual is building up to protect himself—one might well

hesitate at using as an index of the efficacy of treatment what was really the index of the individual's acquired resistance to the disease. The subsidence of the Wassermann at the same time with the improvement in the condition of the syphilitic patient is one of the best evidences that it is independent of antibody and that it is a reliable index of the efficacy of treatment.

So far we are upon reasonably safe ground: the subsidence and disappearance of a positive Wassermann is an evidence of improvement in the condition of a syphilitic, and as such is an evidence in favor of the efficacy of the treatment which he is undergoing. But it is only one piece of evidence; it is not conclusive and compelling evidence that all is well; its value may be completely offset by the persistence of hyperplastic glands, by the persistence of cachexia, or, as at times may happen, the Wassermann-unheralded appearance of mucous patches or a late secondary eruption or a gumma. Its proper value then is as one symptom. It is, however, one symptom of great practical importance because it may be elicited when all others have disappeared. But as an index of the condition of a syphilitic patient or of the effect of treatment it is not entitled to preponderating consideration. It is desirable to see it disappear, as it is any other symptom of syphilis; but it is also desirable that adenopathy should subside, that mucous and cutaneous and systemic symptoms should disappear, that weight should be maintained, and that the patient's feeling of well-being should be high. If some of these evidences of the disease persist or recur we are in no position to say that the patient is better off than he would be with a persistent or recurrent positive Wassermann.

To repeat then, a negative Wassermann is an evidence of the betterment of syphilis, but it is only one form of evidence, and in weighing its importance as an index of the efficacy of treatment it is entitled to weight only in its relation to all the facts in the case.

The fact that the Wassermann is not all-important is no reason why it should not be taken at frequent intervals during treatment and given reasonable weight. And there is good reason to believe that the sooner it becomes negative and the more constantly and longer it remains negative the better is the prospect of the case, as it is with a similar course of all other symptoms of syphilis.

How long must the Wassermann remain negative before we may proclaim a patient cured? We are in no position to answer that question by any positive statement. There is now a very strong pretension that undertakes to claim a cure of syphilis after the Wassermann has remained persistently negative for a certain length of time. There is some justification for this in the abortive treatment of syphilis, when, after the chancre, neither a positive Wassermann nor any other evidence of syphilis appears. Omitting,

however, these cases the clinical history of syphilis compels us to believe that we cannot give a positive assurance that the disease has gone never to return. We can give assurance after several years of a negative Wassermann, of probable immunity, as we can after several years of symptomatic freedom.

How long then shall the Wassermann be taken? If one is to be logical, as long as one's clinical judgment indicates that the syphilitic should be watched; and in my opinion that means at intervals for life. Bayly, himself a pathologist, considering the question from the theoretical standpoint, gives under what seems from the phrasing of the last half of the sentence to be logical compulsion a good answer to this question: "A single negative reaction obtained with a serum of a patient undergoing treatment by mercury or salvarsan means little but that the patient is reacting to such treatment. A series of negative results taken at intervals of three or six months after all treatment has been given up is necessary before the patient can be regarded as cured [here he seems to lose heart—W. A. P.], and even then, until twenty years have passed, we cannot be absolutely certain that the disease is completely and permanently obliterated." In other words, we are no more in position now than we have been in the past to ignore the possibility of future relapses in ourluetetic cases.

Space permits of only a brief consideration of the luetin reaction and the prophylaxis of syphilis by inunctions of calomel ointment, but no review of the newer syphilis can fail to mention them.

THE LUETIN REACTION. Noguchi, using a suspension of killed *Sp. pallidæ*, which he calls luetin, has developed a cutaneous test in syphilis analogous to the tuberculin test. It depends upon the fact that in the presence of syphilis a reaction, showing as an inflammatory nodule, appears after the injection into the skin of a drop of diluted luetin in syphilitics who are in a condition of allergy to syphilis. My experience in about two hundred cases tested with Noguchi's luetin, like that of a number of others who have used it, is that it is a valuable addition to our means of diagnosis. It has the essential quality of specificity. The reaction does not occur in other conditions than syphilis, so that with proper care in technique and interpretation it is a reliable evidence of syphilis. It can rarely be elicited in early syphilis, but in late syphilis the reaction is positive in 50 per cent. or more of the cases. And, fortunately, the reaction frequently develops in late syphilis with a negative Wassermann, so that it is a valuable supplement to the Wassermann test.

All considerations indicate that the test is a specific allergic phenomenon due to sensitization of the tissues to the virus of syphilis. The evidence for its being an indication of active syphilis is of the same character as that for the Wassermann, and as a diagnostic test and as a guide to treatment the same considerations

apply to it that apply to the Wassermann. There seems good ground for believing that the luetin test will prove a useful supplement to the Wassermann in both of these functions.

THE PROPHYLAXIS OF SYPHILIS WITH CALOMEL OINTMENT. Metchnikoff and Roux announced in 1906 that syphilis can be prevented with reasonable certainty by prompt inunction of the infected point with 33 per cent. calomel ointment. Their experiments were of such great practical importance that it is surprising the subject has not created wider interest. In substance their findings are: The inunction should be made within eighteen hours at the latest; at twenty hours it fails. The ointment should be rubbed in for a few minutes; in their most critical experiment it was rubbed in for five minutes. Calomel in the proportion of one part to two of ointment is effective.

Their experiments were carried out with scientific accuracy and the strictest care for control, and the results are entitled to respect. Very extensive attempts at the prevention of syphilis based on this method have been undertaken in the United States Army and Navy, and the experience is strongly confirmatory of the value of the method. As it would appear now this very simple prophylactic procedure is one of the most important measures for the control of syphilis that has been suggested. The ointment used by Metchnikoff and Roux in their original experiments was $33\frac{1}{3}$ per cent. calomel and $66\frac{2}{3}$ per cent. lanoline. The ointment which they recommended is calomel 33, lanoline 67, vaseline 10. This base is stiff and it deteriorates. There is no evident reason why any of the ointment bases may not be used as well, particularly benzoinated lard. The inunction should be made soon after suspected infection—within eight hours if possible; the ointment should be rubbed on to the area of suspected infection for five minutes and the surplus left on the surface.

Of course, Metchnikoff and Roux's effort was not the first attempt to prevent syphilitic infection by the use of a mercurial application. The importance of the work lies in the accurate demonstration of the effectiveness of a simple practical method of prophylaxis.

SALVARSAN IN THE TREATMENT OF SYPHILIS. The man who has to do with the treatment of syphilis has never had a greater responsibility put upon him than exists in the question of the use of salvarsan in the treatment of his cases of syphilis. The claims for it have been so strong and the sponsors for it of such high authority that it has been no easy task to exercise restraint in giving one's patients the supposed benefits of it; and yet, there are many considerations which make one hesitate at its administration in the heroic way which has been advocated and which raise serious questions concerning the sum total of its usefulness. Although the time that it has been in use is short, compared with that necessary to get any final knowledge of the ultimate value of any means of

treatment in a disease so tricky as is syphilis, we are already acquiring a fund of knowledge of salvarsan that enables us more satisfactorily to determine its place in the treatment of that disease.

The questions which confront us now in considering salvarsan indicate a different situation from that which we thought we were in when salvarsan was introduced and we had the hope that in it we had an effective remedy for the cure of syphilis. Now the questions are how effective is salvarsan in syphilis? How far can it be substituted for the older means of treatment, and what are the objections to its use? It is no longer *therapia sterilizans magna*, to use one of the striking terms we learned from Ehrlich.

At present the subject of salvarsan in syphilis can be considered from two standpoints: its value as a symptomatic remedy, and its value as a curative agent. In addition we must consider its disadvantages. The disadvantages of it may be taken up first, for they have some bearing upon all considerations of its therapeutic use.

DISADVANTAGES OF SALVARSAN. Salvarsan has proved less toxic than the organic arsenic compounds of which it is the successor, but it must be at once said that it has not been found the safe remedy that it was hoped to be. It has not proved to be wholly parasitotropic and free from dangerous organotropic and neurotropic qualities, to use more of the terms for which we are indebted to Ehrlich. On the contrary it has shown again that arsenic is still treacherous, and that, combine it as we may, it is when used in quantity still dangerous. The minor disturbances from its use—fever, nausea, vomiting, diarrhea, prostration, headache, low blood pressure, temporary cardiac disturbances, transitory albuminuria and the like—may be dismissed with brief courtesy. Some of them are important as suggesting contraindications to the drug, but they are of no practical importance in so serious a problem as the cure of syphilis.

The serious accidents are in a different category. They show that salvarsan may cause death or great permanent damage of important structures. In comparison with the innumerable injections of salvarsan which have been given the deaths from it have been few, but it is true that the literature gives no adequate representation of the deaths which directly or indirectly have been due to it. And many of these deaths occur in the early stage of syphilis—the stage in which death from syphilis itself is excessively rare—and in patients who were vigorous and otherwise healthy; so that the possibility of this occurrence must be weighed in using the drug, especially in the free manner required in attempts at radical cure of the disease. Some of these deaths have been arsenical deaths, with the symptoms of arsenical poisoning, but more of them have probably been due to indirect, and in many cases not well understood, effects of salvarsan on luetic lesions in structures of vital importance. On this latter point—that the deaths are

not directly due to salvarsan poisoning—much emphasis has been laid by salvarsan enthusiasts, although it would not seem a matter of great practical importance whether death is due directly to a drug or to some indirect result of the drug so long as a fatal result ensues. These salvarsan deaths make it particularly important, when vigorous use is to be made of the drug, that its contraindications be borne in mind—a fact which Ehrlich has emphasized from the start.

Of the untoward effects, those upon the nervous system are of the greatest interest and importance. They go through the whole range from the simplest to the gravest nervous disturbances—herpes, herpes zoster, multiple neuritis, paralysis, especially of cranial nerves, disturbances of memory or of orientation, epileptiform attacks. Salvarsan has not shown the affinity for the optic nerve that was such an obstacle to the use of its predecessors, notably atoxyl. Nevertheless, partial or complete optic atrophy from it has occurred numerous times. The acoustic nerve has shown greater susceptibility than the optic and involvement of it is not excessively rare. In some cases great damage both to sight and hearing has been produced. Perhaps the most extreme form of nervous involvement has been fatal cases of hemorrhagic encephalitis, of which several have occurred. Most of the nervous accidents referred to above are, there seems every reason to believe, directly due to the drug, and they show that salvarsan has the old dangerous affinity of arsenic for nerve tissue. As Busse says, these fatalities are due to the treacherous action of arsenic and the dangers are inherent in the new preparations of arsenic just as in the old; the physician must reckon with the possibility of them whenever he uses large doses of any of them.

And this raises one of the most serious questions in regard to salvarsan. Probably the greatest, and certainly the most wretched, uncontrollable dangers of syphilis are the parasyphilitic nervous affections. The nervous system bears the brunt of the untoward effects of salvarsan upon the organism. How is this to affect the parasyphilitic nervous affections? The question would be less serious if salvarsan were quickly excreted and its action on the tissues soon over. It was at first thought that this was true when salvarsan is given intravenously, but the researches of Buschke and his assistants have shown that arsenic can be recovered from the urine and blood for weeks and months, "yes, even for a year," after intravenous injection of salvarsan. And the clinical findings confirm this, for the nerve lesions of the type we are now considering may appear any time from a few days to months after the administrations of the drug.

These patients then are exposed to the danger of long-continued arsenical intoxication, and that this produces degenerative nerve changes the Manchester epidemic of chronic arsenical poisoning as

well as innumerable separate experiences have shown. We have an unpleasant analogy in the effect of alcohol—another drug affecting the nervous tissues—whose persistent use is generally accepted as a predisposing cause of paresis and tabes. We are then in no position to say that this effect of salvarsan on the nervous system may not render it more susceptible to the degenerative disturbances which follow syphilis itself. Professor Buschke, of Berlin, wrote in 1912, "The theory that the intensive treatment with so neurotropic a drug, which remains so long deposited, can favor the occurrence of tabes and paresis cannot lightly be cast aside." And Professor Brocq, of Paris, wrote in January, 1913: "I do not know what it will do for the remote contingencies which we are discussing (parasyphilitic diseases, W. A. P.). We are at liberty to hope for the best, but I must admit that I am the prey of grave doubts." Only long experience can settle this important question.

The other class of nervous accidents following salvarsan are not assignable directly to its toxic effects, but occur through its effect on syphilitic lesions. These accidents may result from the sudden solution through the action of salvarsan of luetic lesions in important structures—a process that probably represents the extreme degree of the Herxheimer reaction. Others of them correspond to the usual form of Herxheimer reaction, that is, the temporary stimulation of luetic infiltrations by the drug, with the production of congestion and edema. If this occurs in meningeal lesions it may cause great temporary increase of intracranial pressure, or if in a cerebral endarteritis it may result in occlusion of the vessels. It is this reaction of active specific lesions to salvarsan—which is explained as due to the sudden liberation of supposed endotoxins—that accounts for most of the comas from salvarsan administered during the secondary period, when mild syphilitic meningeal irritation is likely to exist, and which compels caution in the use of salvarsan in the presence of syphilitic cerebral lesions.

The other form of nervous accidents following salvarsan are true syphilitic lesions in nervous tissues—the "neurorecidives" of Ehrlich, nervous lesions of syphilis, with which we were familiar before the advent of salvarsan. It was vigorously maintained until recently that these nerve involvements were not more frequent after salvarsan than before it came into use. And to support this contention the whole previous study of syphilis was indicted and charged with simply having overlooked them. Now it is admitted that they are more frequent, and this fact is taken into consideration in every scheme of salvarsan therapy. It is one of the facts which have compelled the simultaneous use of mercury. These neurorecurrences will be reverted to in considering recurrences in general.

One can, by dwelling on its dangers, exaggerate the untoward effects of salvarsan. They are relatively infrequent and, because of their infrequency, relatively unimportant in comparison with the great gain of curing syphilis if we have any reasonable assurance of attaining that end by salvarsan.

SYMPTOMATIC ACTION OF SALVARSAN. There can be no two opinions as to the specific action of salvarsan upon the active lesions of syphilis. It is a powerful symptomatic remedy. In rapidity of action it surpasses mercury or mercury and iodides in many lesions; in others, it equals or is inferior to these older remedies. In early syphilis it has a quick effect upon the initial lesion, mucous patches, and condylomas. Its action is quick upon mucous-membrane lesions generally. Its effect upon the cutaneous eruptions is not more prompt and not more complete than that of mercury. Upon the severe forms of early syphilides—large pustular eruptions, early gummatous lesions—its action is often strikingly effective. According to wide experience the effect upon the adenopathy of syphilis is surprisingly slight. Upon late gummatous lesions of the skin—apparently less upon gummas of the internal organs and upon bone lesions—the action of salvarsan is usually prompt and effective. It is in extensive and intractable lesions of this sort that it has probably its greatest field of usefulness as a symptomatic remedy; and it is the more promising here because, for the healing of such lesions, moderate doses are sufficient and the use of heroic quantities of the drug are not necessary, as in the attempts at radical cure with it. In the rare cases of severe early or late syphilis, which are not amenable to established methods of treatment, it undoubtedly is an effective addition to our means of treatment.

Aside from these latter and rare cases there is need to emphasize that salvarsan, as a rule, does nothing in gummatous lesions of syphilis that cannot be done effectively with mercury and the iodides—perhaps done slightly slower, but almost without any of the toxic dangers of salvarsan. For there is a tendency now to forget the value of the older means of treatment of these lesions. And so we constantly see reference to cases “hopeless by mercurial treatment,” “intractable to mercury and iodides” or “malignant.” As a matter of fact such cases, in which actual lesions of syphilis, not parasymphilis, are uncontrollable by mercury and the iodides and rational measures are excessive rarities. The treatment of such lesions by mercury and the iodides is, as a rule, one of the most definite feats of therapeutics.

As to the effect of salvarsan upon the Wassermann, evidence is conflicting. Experience in general is that except in the early primary stage it is not more effective in reversing a positive Wassermann than is mercury; in moderate doses it is less effective than safe vigorous mercurial treatment.

CURATIVE USE OF SALVARSAN. What of salvarsan as a cure for syphilis—the high result that was hoped for when it was introduced? How far has it realized this hope?

In the primary stage, at the appearance of the chancre, the evidence is strong to lead us to hope that with salvarsan much more can be done than has ever been done before to abort syphilis: That is, when the syphilitic patient is seen before the disease has become generalized, while the spirochetal infection is localized around the initial lesion and before the Wassermann has become positive, it is possible in many cases to prevent the development of secondaries and hold the Wassermann negative by immediately instituting and vigorously carrying through a course of salvarsan and mercury treatment. The period of observation of these cases is still short, and success in preventing all early indications of syphilis is not conclusive proof that the patients are free from syphilis; but it is more than we can do with mercury, and it is strong presumptive evidence that the disease has been aborted.

This abortive action of salvarsan in the primary period gives it a very valuable field of usefulness. As already indicated, about 40 per cent. of cases of initial lesion, which can be distinguished by the demonstration of the *Sp. pallida*, show a negative Wassermann for one or two weeks after the lesion's appearance. In these cases there is a reasonable prospect that syphilis can be aborted—a prospect that justifies a vigorous attempt with salvarsan. This of course makes the early diagnosis of the initial lesion a matter of great importance.

After this brief stage of promise has passed the prospect of cure rapidly changes. It becomes less promising from week to week, and after secondaries are well established it almost or quite vanishes. That sad conclusion has been forced upon us by the accumulated evidence of recurrences in cases treated in the secondary stage. It has gradually forced the salvarsan advocates from the use of a single massive dose to courses of many repeated doses in combination with the most vigorous mercurial treatment. There the method now rests. In the opinion of salvarsan advocates some early cases can be cured by vigorous treatment. But even they admit that if cure is to be attained it is only by heroic courses of salvarsan—2 to 4 grams of salvarsan in a few weeks—combined with vigorous intramuscular use of mercury. If less than this heroic attempt at cure is made the opinion, even of some salvarsan advocates, is coming around to the view that the drug had better not be used at all. Some have gone even farther and do not use it for curative purposes after the Wassermann has become positive.

This position I believe is one which we are forced to by the logic of experience. And this position, quite aside from any hesitation about using the drug on account of its dangers, depends upon one fact—the increased frequency of severe syphilitic relapses, chiefly

nervous, after the use of salvarsan. That there is an increased frequency of relapses of syphilis in the form of nervous lesions is now accepted. This is true as well, I believe, of relapses of gummatous lesions in the skin and elsewhere, but attention has been centred upon the nervous lesions because of their seriousness. Attention was early called to the frequency of nervous lesions after salvarsan by Finger, Rille, and others. The fact was bitterly denied by Ehrlich and his school, Benario, with industrious loyalty, going so far as to compile in a book the cases of nerve syphilis in the literature of presalvarsan days in order to show that their frequency is not now greater than formerly. But from that position they have been compelled to recede, and now the increased frequency of "neurorecidives" is admitted even by salvarsan enthusiasts. Thus Nichols and Hough, Nichols being one of the earliest and still one of the most enthusiastic salvarsan advocates, say: "The question still remains why these relapses are more frequent under treatment with salvarsan than with mercury."

Much difference of opinion has existed as to the reason for these relapses, some attributing them to the direct effect of the arsenic on nervous tissue, Ehrlich's school vigorously maintaining that they are lesions of syphilis. There is little doubt now that the latter view is correct, and in the reason therefore lies the strongest indictment to be made against salvarsan.

To complete the quotation from Nichols and Hough: "Some authors hold that salvarsan damages the nervous system and thus predisposes to a localization of the spirochetes in this region. It seems to us, however, that these relapses can be satisfactorily explained according to Ehrlich's ideas. In a considerable number of cases in the secondary stage the nervous system is infected with or without symptoms. . . . When such a case is treated with salvarsan the great bulk of spirochetes are suddenly destroyed. They are not simply repressed, as is the case under mercury, and the resistance of the body is not gradually stimulated against them. There remain, however, small foci of spirochetes, especially in areas which are less accessible to the circulation, such as are found in the central nervous system. After a time these spirochetes begin to multiply, and they meet no resistance such as is afforded by the continuous administration of mercury or by the natural defences of the body, because these defences have not been continuously stimulated by a large number of organisms all over the body. As a result the spirochetes which have remained grow with increased vigor and presently produce symptoms where they are located, in the nervous system." And as we would expect if this last phrase were stated in the full form logically demanded by the "increased vigor," the spirochetes, growing without the opposition of the usual resistance developed by the infected organism, cause new lesions of severer type than is usual in early syphilis.

Stated in another form this proposition is as follows: Salvarsan destroys the spirochetes except those walled off in inaccessible localities; therefore, the body is not stimulated by a general infection to the production of those antistances which are its natural defence, and so builds up little or no resistance. Later these isolated foci of spirochetes grow, and because of lack of acquired resistance to them grow with increased vigor, and so produce damaging lesions. Finally their growth spreads beyond the isolated focus or foci and, as after the chancre, infection becomes general, while at the same time no natural defence has been built up. In other words, the patient who is treated vigorously with salvarsan but short of absolute destruction of all the spirochetes has his day of reckoning briefly postponed, but at the price of having to meet it later under adverse conditions.

This is why the view is gaining ground that if the prospects are not good of cure from salvarsan, or if it is not to be given in the vigorous way necessary to have a chance of cure, it had better not be used at all in the early period of syphilis when the patient is building up his natural resistance.

This reasoning of course does not apply against its use as a symptomatic remedy for the treatment of the later lesions, long after the patient's specific immunity has been stimulated and utilized.

TO RECAPITULATE: 1. Salvarsan has real dangers; they are remote, but, when they occur, serious.

2. As far as can be deducted from our present knowledge there is no reason to believe that salvarsan will lessen the occurrence of parasyphilitic nervous affections, and some ground for fear that it may predispose to them, except in those cases in which it cures the disease.

3. It is a powerful symptomatic remedy.

4. In cases in which vigorous treatment is begun before the generalization of the disease there is strong ground for believing that syphilis can be aborted. This possibly applies to a few early cases with secondaries.

5. In all other cases in the secondary period its "curative" use may do more harm than good.

"Whatever be the power of the new arms which have lately been placed at our disposal for the treatment of pox, the practitioner must clearly understand that the antique rules of therapeutics have not undergone any change. He must grasp the idea that his duty is first and foremost to place the organism in the best possible state to resist and thus minimize the virulence of the infection; that by a well-ordained hygiene he may reduce to a minimum the secondary manifestations and the tertiary liabilities." (Brocq.)

THE HEART IN SYPHILIS.¹

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ABOUT one year ago I reported before the Society of the Alumni of the City Hospital a systematic anatomic study of the heart and aorta from fifty consecutive autopsies in cases of syphilis. I was stimulated to this investigation by the frequency with which I had observed serious and often fatal circulatory symptoms in cases of lues, many in patients who had been well treated and who not infrequently had long before ceased to manifest any signs or symptoms directly attributable to syphilis.

This study led me to believe that luetic involvement of the heart and aorta is much more frequent and much more serious in its direct effects than has been generally conceded by internists or even by syphilographers. In many text-books and monographs on this now newly understood infection, syphilis of the heart is not uncommonly mentioned as among the more unusual complications of the disease; yet in my postmortem series I find that 66 per cent. of my luetic cases, including well and incompletely treated instances, die as a result of or with serious circulatory disease apparently of specific origin. On analysis I find that in many reports this apparent infrequency of cardiac involvement is probably based on the relative rarity with which one finds true gumma in the heart at necropsy. In the other viscera the liver, the kidney, or brain, we also count as luetic the scleroses, fibroses, and degenerative changes which follow the more active syphilitic lesions.

Applying this same general basis for syphilitic cardiac lesions in my anatomic study of 50 cases, I found the following relative occurrence of definitely specific changes. The epicardium or visceral pericardium was diseased in 28 of the 50 instances. In regard to this membrane I call particular attention to a somewhat characteristic lesion manifested grossly by the appearance of opalescent patches of thickening which correspond to the perforation points of terminal arterioles. These opacities are formed of a mingled fibrous and endothelial hyperplasia which apparently occurs chiefly about the terminal arterioles. This lesion is not confined to lues but is much more frequent in it than in any other one condition which I have yet observed, and I have compared its genesis to that of syphilitic leukoplakia so frequently seen, especially in the buccal mucosa.

The myocardium was found diseased to a serious degree in 44

¹ Read before the Internal Section of the Buffalo Academy of Medicine, December 10, 1912.

of the 50 cases, and true cardiac gumma was present in 5 instances, a percentage of occurrence closely approximating that given by Marcek. The most frequent myocardial change was found to be an inflammatory process manifested in the greater number of my cases, which were chiefly of late stage syphilis, by small round-celled infiltrations about the arterioles or by foci of fibrosis which I believe to be results of the inflammatory or infiltration process shown in the first-mentioned lesions. As a probable sequence of such changes, cardiac aneurysm was found present in 3 instances. Diffused or localized areas of scar formation were frequently encountered, but fibrosis was usually associated with other changes, often degenerative in character. Acute purely degenerative lesions were absent except in certain examples where they had apparently resulted from concomitant or independent disease.

In 35 instances disease of the coronary arteries was present to a relatively greater grade than the general arterial changes. This specific affinity to attack the coronary vessels has long been recognized, and in certain of my group of cases it was shown to have become an important factor even before the secondary rash had fully declared itself. The occurrence as well as the degree of coronary disease appears to correspond more or less with the activity rather than to depend on the duration of the infection. In this regard also it is interesting to note that age apparently plays little if any role in the determination of coronary disease in lues. Five of my most striking cases were below thirty years of age and 4 others below forty.

The type of the coronary change is variable. In 3 instances coronary thrombosis had resulted from an active primary endarteritis, but the most frequent change appears to be a fatty degeneration with endarteritis. From the diseased vessels there spreads out into the muscle all manner of changes, from a granulomatous and true myocarditis to fibrosis or necrosis, the result of deficient nourishment. In 2 examples of my autopsy series, aneurysm of the aortic arch was found present within six months after the primary lesion.

The natural questions which occur to a clinician after finding changes of this kind so prevalent are: When do they occur? Do they produce symptoms and signs which are clinically recognizable? May these lesions be prevented? May they be cured?

During the past two years my clinical studies have been largely directed toward an attempt to answer for myself these queries. Partly through the courtesy of my colleagues I have been able to carefully study in my own services a large group of cases of tertiary syphilis which directly applied to this subject and through the generosity of my colleague, Dr. J. A. Fordyce, of the syphilis service at the City Hospital, I have also been enabled to observe

numerous cases of primary and secondary lues both before and after treatment.

It is manifestly impossible to go into accurate statistical or analytic details in so generalized a paper as this, but I hope to cover the ground of our studies in a sufficiently comprehensive manner to give a general idea of the conclusions which we have thus far reached. My associate, Dr. Carroll, and myself hope to publish later in considerable detail the various phases of the subject as they have appeared to us after a still wider and longer-continued experience along these lines.

As to the time when changes of a serious character appear in the heart. In many cases of aggressive onset during the secondary symptoms, irregularities of heart action appear; exercise, such as double time for sixty seconds, will frequently produce intermittence, extrasystoles, and other disturbances of rhythm. Abnormally rapid action is common and under stress; a soft systolic mitral murmur may appear. In brief the symptoms of heart deficiency at this stage are precisely such as at times appear in the febrile stage of most infections, such as typhoid, rheumatic fever, septicaemia, and the like. One might fairly assume from this fact that the changes in these instances are precisely such as appear in any infection, and such I believe is the prevailing opinion. In a few instances, however, death has taken place, and autopsies have demonstrated these manifestations to be due to typical syphilitic inflammatory alterations in the heart muscle or in its arterioles. Three such cases have been studied by me.

In one case of my series which terminated unexpectedly before the secondary rash had fully appeared, and before the diagnosis had been made, death immediately resulted from a minute perforation of the wall of the aorta, just above the ring. A pronounced acute arteritis and periarteritis was found throughout the myocardium, particularly involving the vasovasorum of the aorta. Large foci of round-celled infiltration, with parenchymatous degeneration of the muscle cells and an active hyperplasia of the connective-tissue interstitium, was found—all typical and unmistakable syphilitic changes, yet they appeared in the early secondary stage of the disease.

Grassman records similar observations, and since I believe that I, with others, have demonstrated that these specific inflammatory changes develop first in and about the arterioles of the heart muscle, we cannot then assume other than that serious involvement of the heart may begin before or with the secondary stage of the disease. Obviously the postmortem evidence of this fact is not large, because cases now rarely die in this stage of the infection when nearly all patients are more or less effectively treated, one must therefore rely largely on clinical evidence for the confirmation of this fact.

Several cases in the active early secondaries which were seen by us in the service of Dr. Fordyce, and which showed unmistakable evidences of myocardial disease, such as tachycardia, extrasystoles, murmurs, and other irregularities of tone, rhythm, and force, when submitted to vigorous antisymphilitic treatment, showed within three days the disappearance of these signs, and all symptoms of cardiac disease vanished without resort to circulatory measures except rest in bed. Such cases, together with the postmortem evidence which I have been able to collect, satisfactorily indicate to me that early syphilitic lesions frequently appear in the heart, that they may be serious, and that they then cause symptoms of a sufficiently definite diagnostic character.

Now that the spirochetes of syphilis have been demonstrated in the heart muscle lesions of this type,² there remains no argument as to the specificity or significance of the lesions. It is inevitable that there should follow them changes of a more or less permanent and often grave nature.

If, as I believe my previous study has indicated, the changes in the heart chiefly originate in and about the bloodvessels, it is plain that the onset of the changes in the heart should occur early, for there can be no doubt but that we have an early septicemia or lymphemia in syphilis. Therefore it seems fair to assume that cardiac lesions are to be expected among the earliest of all visceral disease in this infection.

If we are then correct in this assumption, from the nature of the heart physiology, the largely unregenerative character of the heart muscle, and the inevitable fibrotic alterations which must succeed myocardial discrepancies, it follows that energetic treatment is imperative immediately after diagnosis in lues if for no other reason than because of the almost certainty of cardiac invasion. Fortunately it is no longer a question in therapeutics as to when treatment should be instituted in syphilis, and since this point has been satisfactorily settled, I have no doubt but that fewer cases of death as a result of luetic lesions of the heart will be reported.

As to the signs and symptoms which appear in syphilis as an indication of involvement of the heart, much work still remains to be done. As we have already remarked the most frequent and earliest lesions found are arterial or myocardial ones, and we all recognize the difficulty of absolute diagnosis of either of these conditions even when they are fully established—small wonder then that the early signs and symptoms of syphilitic involvement of the heart are neither clear, definite, nor characteristic.

Insofar as our personal observations go, the earlier symptoms

² Buschke and Fisher, *Deutsch. med. Woch.*, 1906, Nr. 19; Simmons, *Münch. med. Woch.*, 1906, S. 1550.

are irregularity of action, more marked when strain is added, as by mild exercises or through nervous apprehension. Rapidity of action is also present in most cases, and it is incited to a degree and by conditions which in the normal would fail to elicit such a response. Pain and tenderness in the region of the heart demonstrated with or without heavy pressure over the precordium is present in a few of the early cases. I believe that these symptoms appear chiefly or only when extensive inflammatory lesions are present in the muscle or when dilatation has developed. I know, however, from clinical and postmortem evidence that pain and tenderness are not invariably present even in cases where actual cardiac aneurysm has developed. In no instances have I observed any significant alterations in the blood pressure except secondary modifications, when obvious decompensation was present, or in advanced cases when some such concomitant conditions as a nephritis complicated the picture. Neither have I observed any other characteristic alterations in the pulse in the early stages except the irregularity of rhythm and force already remarked. If I may be permitted to so express it, the characteristic of the irregularity of action in the early cases is its irregularity—its lack of system. I have never as yet observed anything indicative of a heart-block or auricular fibrillation in the early phases of the disease.

In the latter stages of the condition, that is, in the tertiary and quaternary periods, the signs and symptoms of cardiac disease naturally become much more certain, though rarely in my opinion definitely indicative of lues—the signs and symptoms of the case become rather those of a myocarditis, of a cardiac aneurysm, of heart-block and the like. For this reason the specific etiology is likely to entirely escape detection. Symptoms and definite signs of cardiac disease may be absolutely absent, as shown in several instances which came unsuspected to autopsy when marked lesions were found. One cannot therefore assume that cardiac complications are necessarily absent in any case of syphilis because signs and symptoms are lacking.

Of the manifestations which appear with the greatest frequency in long-standing cases of lues, I believe that irregularity of action, especially when under strain or stress, is probably the most frequent, as it is also in the earlier stages. With the irregularity of action often appear murmurs or the accentuation of preëxisting murmurs or other alteration in their character. As we have already remarked in the early stages, murmurs are not very frequent, though they may appear; but in the long-standing cases they are frequent. Analysis of my postmortem cases shows a definite endocarditis present in 74 per cent.; 14 per cent. of the aortic ring; none of the mitral alone but 34 per cent. of both aortic and mitral. In many instances activity was still manifest, particularly in the aortic cases.

In advanced cases, as in the acute, pain in the region of the heart sometimes with tenderness is not infrequent; but here it is commonly of an anginal character, and reflected to either pectoral region, into the back, or down the arms. We have been able in most marked examples of this sign to satisfy ourselves that the symptoms of pain and tenderness were associated with dilatation, and is such as may occur in any type of myocardial degeneration after exercise. It is not infrequently entirely relieved by the administration of digitalis or strophanthus, and I am inclined to assume that in such cases pain is really caused by the dilatation, though this in turn may be due to coronary disease. I have seen several instances of undoubted angina pectoris, with or without dilatation, relieved by specific medication, and therefore consider them probably luetic in nature. None of these cases have come to autopsy, and are therefore not capable of absolute proof.

Stokes-Adams syndrome has been frequently reported as a result of syphilitic or gummatous myocarditis. During the past two years 5 of these cases, all history and Wassermann positive, have come to my notice, 2 in hospital and 3 in consultation with other physicians. Although in all these, tracings and in 2 electrocardiograms, also, showed the rhythm to be typical of heart-block, syncopal attacks have appeared in but 1. One hospital case, alternately under the service of Dr. Oppenheimer and myself, a man, aged seventy-eight years, has no disturbances whatever, but goes about the wards complaining of nothing except the natural disabilities of his age. It is important to record in relation to the role which lues plays in heart-block that these 5 cases have all been submitted to active antisymphilitic medication, but it has in no way altered the block, although in 2 cases the symptoms of dyspnea, cardiac pain, and of defective capillary circulation have been greatly relieved. So far as I have been able to ascertain no cases of heart-block have been recorded in the acute stages of syphilis. Several investigators record improvement under modern methods of treatment in late cases, such as mine, but we have not been thus fortunate.

It can safely be said that in the tertiary stages at least there are no definite pathognomonic signs or symptoms of syphilitic involvement of the heart. Diagnosis must in most instances rest on the discovery of a cardiac lesion, which is not accounted for otherwise, and a response to the Wassermann reaction. I do not wish to be misunderstood to indicate that I consider the Wassermann reaction infallible, either in a positive or negative sense, but I do consider it as yet the most definite sign in the diagnosis of syphilis in the later tertiary or quaternary stages, especially if the case has been more or less well, though incompletely treated.

In the diagnosis of heart involvement in syphilis a serious impediment is placed in our way in regard to history. According to my

hospital statistics, based on confirmation by autopsy, only 30 per cent. gave a positive history. From my private records the percentage of positive history is here even less frequent. A certain number of these cases, more in private than in hospital practice, deny luetic history even when the truth would much better serve their purpose, and on the other hand, through lack of intelligence or observation, a considerable number of hospital patients overlook symptoms which would be observed by the more intelligent, and which when recited would definitely identify the condition.

Finally, I believe that the most definite and only certain criterion in a diagnostic way in cases of cardiac disease in lues is a betterment or cure of the conditions under purely specific medication. This has acted very satisfactorily with me in several instances of presumable syphilis, where the history and physical findings were doubtful and the Wassermann reaction inconclusive. To apply the therapeutic test in these cases does not appear any more unscientific to me than the administration of specific drugs in tumor of the brain, under the supposititious diagnosis of gumma when even the Wassermann is negative or indefinite.

While from the foregoing it must appear that the signs and symptoms of cardiac involvement in lues are indefinite, it will be granted that they are little more so than are those of most types of myocardial disease; but when signs and suggestive symptoms, especially with actual endocardial murmurs, appear without other likely cause, then the diagnosis either with or without the assistance of a history or a Wassermann reaction becomes quite sufficient. Several instances have appeared in my services in which the sudden, unexplained, and afebrile onset of an apparent aortic endocarditis has acted in a highly diagnostic way; in some such examples little opportunity for error exists.

Little need be said as to the progress of the involvement of the heart in lues once it has originated. The great frequency with which it terminated either fatally or in lesions which absolutely disqualify the patient from playing a normal part in the world's work is obvious to all who have considered the subject. Cases also exist with little or no disturbance even when extensive and serious lesions appear postmortem. We have found in our hospitals that a surprising number of cardiac cases in which the etiologic factors were obscure or entirely undiscovered, either responded to a Wassermann or on careful inquiry gave a history which justified the introduction of an antiluetic treatment, which was followed in a number of instances by such improvement that it could not be considered as otherwise than confirmatory. So general has been this result that we have frequently found it advisable to apply this therapeutic test even in cases historically and serologically negative.

As to the question whether the involvement of the heart may be

prevented in lues. An absolute answer is at this time difficult, because a sufficient number of cases which received vigorous and protracted treatment in the early stages of the infection have not as yet remained sufficiently long under observation to justify definite conclusions in this respect. This much, however, must be admitted in the acute cases: That those in the active, aggressive, and progressive periods of the secondary stage which have been treated by modern methods have thus far shown no recognizable cardiac complications. Furthermore, as before stated in cases where cardiac lesions or symptoms had appeared and vigorous methods of treatment were applied, disappearance of these signs and symptoms has followed in most cases.

Unfortunately this is a line of work which it is unlikely that I shall be able to follow out because most of the cases which come to an internist are not in this period of infection, but are in the late tertiary stage. Perhaps I may, however, be pardoned for stating in this not inapt place my belief founded on my studies in pathologic anatomy that an attempt to divide syphilis into periods or stages is unsound pathologically and unsafe clinically—one commonly finds so-called tertiary lesions appearing in the secondary stages of the disease and from time to time in the tertiary period, sudden and aggressive exacerbations of the process spring up which can be only compared to those which we are accustomed to ascribe to the secondary stage. There is no essential difference, except in degree or size between the granulomatous processes of the secondary stage and the gummas of the third period.

It is a curious fact that although we have recognized since the days of Paré that syphilis caused disease of the heart, and that aortic disease in particular was frequently caused by it, we have apparently not appreciated until recently that these syphilitic manifestations should receive the same recognition and treatment which has in the past as in the present given such brilliant results in the treatment of syphilitic lesions elsewhere.

Collins and Sachs,³ and Longcope, in 1910, called attention to the good results which follow the treatment of syphilitic lesions of the heart, just as like changes are managed when they appear elsewhere in the body. But few text-books as yet, however, point out the frequency of the complication or the necessity of adopting in it the same energetic line of treatment used in other forms of lues. Few practitioners apparently appreciate the results which may be reached by this means or the serious termination which is practically certain to follow in case no adequate treatment is instituted.

As an illustration of these features I wish to cite briefly the following case:

³ Trans. Assoc. Amer. Phys., 1910.

Ten years ago a well-known colleague, in the course of his work, acquired a chancre in the end of the nose. Vigorous mercurial and iodine treatment had been promptly instituted under the supervision of an eminent syphilographer. Prompt disappearance of the obvious signs and symptoms of this disease took place, and the patient, himself an authority in this branch of work, continued the treatment for a period of two years, after which no evidences persisting, treatment was dropped. After a severe season of heavy work, early this past summer, he noticed that his heart intermitted, that some dyspnea was present on slight exertion, and an oppressive pain was almost constantly present in the region of the precordium. I found on examination that the heart was irregular, that the action became markedly intermittent on slight exertion, with the appearance of extrasystoles and of slight cyanosis and pallor. Auscultation showed the presence of a soft apical systolic murmur, not transmitted toward the axilla but upward over the sternum. A distinct systolic murmur was found at the aortic area transmitted into the vessels of the neck. The cardiac area was not increased, but heavy percussion over it caused discomfort. The Wassermann reaction was next day found strongly positive, but without waiting its determination the patient was the same day given 0.6 gram of salvarsan intravenously. A considerable reaction followed, and for several days the patient was seriously ill, with pains in the muscles and bones, high fever, and rapid pulse. Nonetheless, inside of one week the murmurs had decreased in intensity and the heart had become more regular and forceful in its action, and by the time that he was able to be about the cyanosis and dyspnea had vanished. Mercury was then administered and the patient has since remained under careful observation, though he is now able to continue his large practice. Two months later the intermittence had entirely disappeared, and after four months no heart murmurs can be found even after exertion.

As to the best methods of treatment. Although I do not feel that sufficient time has yet elapsed for me to draw definite conclusions from the cases which I have had under observation, certain facts have, however, come out which I believe may be of value to others, since some of them have been learned by me at the expense of considerable worry.

I may begin in this respect by the statement that so far as my experience goes the special type of treatment must be determined by the results on the patient—there is no other adequate measure. No two cases permit of identical methods. It is at present my chosen method of treatment to confine the patient to bed when the signs of cardiac disease are such as would suggest this step independent of the question of syphilis, but not otherwise. I believe that we have in the past been perhaps too frequent in our

use of the bed in the treatment of all manner of circulatory disturbances. Many patients, especially young persons, do better if allowed up, with restrictions, of course, especially in the direction of excitement and exercise; entire suppression of muscular effort in my opinion is usually contraindicated.

If the indications of cardiac discrepancy demand it I give digitalis, morphine, strophanthus, or what other drug is apparently indicated by the condition and symptoms of the patient. In brief, I treat the case primarily as one of primary circulatory disease. I then begin the use of mercury, and my general preference is for the salicylate administered hypodermically in sterile albolene. I push this drug until definite but not poisonous indications of its effect are reached, afterward decreasing or intermitting its administration. In some cases mercurial inunctions appear more desirable, in other mercury by mouth; and I have at present a patient under my care who tolerates it only when administered in the old-fashioned vapors; speedy progress without discomfort having followed since this method has been adopted. I do not give the iodide in this period of the treatment, though I know no reason why it should not be so employed by those who have confidence in its specific action.

After the case has thus been under observation and treatment at least for a few days, in suitable instances, I recommend the use of salvarsan, not because I consider it indispensable, nor because I think it a more certain specific than mercury in the management of circulatory involvement in lues, but because given in the customary doses it has in most cases a more rapid effect than mercury alone. I believe that it affects some cases in which mercury seems inert, and also in the average patient I follow it up by the resumption of mercury.

In this form of syphilis, salvarsan is best administered intravenously. I have tried both methods, and my earlier preference was for the deep muscular injection. I am still of the opinion that this method may possibly give the most lasting effects in the disease, but that is not what I elect to use salvarsan for in the cardiac complications of lues, but for its quick effects and especially for its direct and speedy action on the bloodvessels and their immediately adjacent tissues. Added to this are the occasional foci of necrosis or abscess formation which may follow the intramuscular method even in the practice of the most careful technician, if he but continue the method long enough—a statement which a few months ago I might perhaps have questioned, but not so now. As to the special method of intravenous administration I have little to say; most of my cases have received the treatment from my associates, interested purely in syphilis, and I have therefore had cases managed by various technical methods. I have no preference for either the one or the other, and I believe that the best method is that with which the operator is himself most familiar.

At first I was accustomed to administer the full dose of 0.6 gram at one sitting; that is, for fully developed adults; following this up later by other doses if necessary, and by energetic after-treatment with mercury. Although I still maintain that theoretically this is the preferable method of treatment, acting on the basis of the theories in regard to its action, experience has shown that this is a dangerous procedure, and three cases so treated under my advice have nearly died as a result of the drug and its after-effects.

One of these cases which I saw with Dr. Wren I shall never forget. It was that of a small but previously vigorous man who had contracted his lues some twenty years before, and who had been treated at that time by the usual methods in vogue. He had since lived liberally in all respects, but without any apparent return of his syphilis. He had meanwhile acquired a family of three persons, and had carried on a large and important law practice.

When seen he was suffering from marked dyspnea, especially on slight exertion. Dilatation of the right and left ventricles was present. Both auricles were dilated. The heart action was irregular and intermittent at times; auricular fibrillation was perhaps present, though a satisfactory polygraph tracing could not be obtained. Most of the time he showed a typical heart-block, with periods of characteristic attacks of syncope. The recent history abounded with frequent seizures of this syndrome. I agreed in advising the use of salvarsan, and soon after the drug was given intravenously by a careful, experienced, and thoroughly reliable operator. Soon after the injection the ventricular contractions dropped to ten per minute; the patient became unconscious, went into collapse, and apparently became moribund. Only the most vigorous and persistent treatment saved his life, and he was for a long time thereafter gravely ill. The arsenic was in this case followed up by mercury, with relief of his cardiac distress and of most of the other signs and symptoms as well, but the heart-block has persisted. He has been able to resume his practice. No more salvarsan has been given, both because the doctors were not anxious to repeat their experience, and also because the patient absolutely refused to repeat the treatment, especially as he is now comfortable and apparently progressing under mercury and the iodides.

A further case illustrative not only of the dangers and benefits encountered in the treatment of cardiac syphilis by means of salvarsan and also of the manner in which the drug acts is probably worth recording in brief, particularly because of its characteristic history and the immediate bearing on the manner in which the drug affects the cardiac tissues in these cases.

The patient, a male, aged sixty-three years, entered my service at the City Hospital in February, 1910. He was a cook, formerly

a soldier in the Prussian Army. He was married, but had had no children. He came of a healthy and long-lived family. His juvenile history was unimportant. He had rheumatism ten years previous to entering the hospital, and typhoid fever seven years ago. He was a moderate user of alcohol and tobacco. He denied not only the history of venereal infections, but also of all skin or mucous membrane symptoms which might be construed as of possibly syphilitic origin.

His chief complaint was of shortness of breath, especially on exertion. This symptom first gradually developed about one year before his entrance to the City Hospital, and was associated with pain in the precordium, headache, and swelling and cyanosis of the hands and feet. He lost between fifty and seventy pounds in weight during this time.

A summary of the chief points brought out by the physical examination were marked dyspnea on exertion, marked cyanosis of the face, hands, and feet, together with considerable edema of the hands and feet. The right pulse was small and indistinct, and was absent for most of the time. The left pulse was regular, the artery plainly palpable and thickened. The respiratory movements were shallow, rapid, and accompanied by sibilant rales, usually apparent even without direct auscultation.

The apex beat was visible and palpable in the fifth interspace, and four inches to the left of the midsternal line. The right cardiac border lay one and a half inches to the right of the midsternal line. The heart sounds varied greatly in rhythm, and in the occurrence, disappearance, and location of murmurs. The thorax presented considerable bulging and enlargement of the left side. Percussion demonstrated the presence of a broad area of dulness beneath the manubrium sterni, but no tracheal tug or abnormal suprasternal pulsations were found. There was enormous distention of the superficial thoracic veins which anastomosed below with the radicles of the superficial epigastrics. This venous anastomosis was especially definite on the left side of the body where the superficial veins of the arm and forearm were also much dilated.

The liver dulness was found to extend about a hand's breadth below the costal margin. The liver was firm on palpation, but somewhat tender. The spleen was enlarged, easily palpated, and tender. The abdomen contained considerable fluid.

Examination of the blood showed a constant polycythemia. The urine showed the continuous presence of albumin, casts, epithelial, and occasionally blood cells. The amount varied greatly, depending apparently on the condition of the circulation.

A diagnosis was made of aneurysm of the transverse arch, myocarditis, cirrhotic liver, and spleen, with secondary nephritis and polycythemia. Radiographs verified the diagnosis of aneurysm or aneurysmal dilatation of the transverse arch of the aorta, and

because of the size of the sac, with its non-pulsatile character, it was assumed to be filled with laminated clot.

Syphilis was assumed to be present because of old skin lesions and the lack of other explanatory causes, but the Wassermann reaction was first reported negative, but later, after treatment had been instituted, it was several times found to be strongly positive.

Some relief was at first experienced from rest, the use of digitalis, and of the other usual cardiac drugs indicated in such cases; but he began to relapse as soon as he was allowed out of bed and about the ward. He developed from time to time hydrothorax, foci of bronchopneumonia, and attacks of pleurisy. Marked abdominal ascites and general edema appeared, and from time to time suppression of the urine, grave dyspnea, precordial pain, and other evidences of circulatory incompetence.

Mercurial medication was attempted first by mouth, then hypodermics of the salicylate, and finally, by inunction. These measures failed to give relief, and as he promptly developed under each early symptoms of mercurial poisoning attempts at treatment with this drug were suspended. Both massive and small doses of iodide of potassium were then prescribed, but he promptly developed a profuse pustular rash, began to run temperature, and this was also given up.

The patient was slowly becoming worse in every respect; the edema had become great, the urinary secretion small, and he passed into a comatose condition from which he could not be aroused by hot packs, cardiac stimulation, diuresis, and the other usual measures. Hitherto we had hesitated to give salvarsan because of the precarious condition of his circulation, fearing a Herxheimer reaction, which might terminate the picture. Finally, as death seemed to be but a few hours distant, it was determined to attempt the drug; 0.3 gram of old salvarsan was injected slowly into a superficial vein. The respiration stopped and he was thought to be dead. Venesection gave a sluggish flow of greatly cyanosed blood. Salt solution was injected intravenously, the extremities elevated and bandaged, adrenalin, camphor and ether, strychnine, and digitalin, were administered hypodermically, and the patient slowly rallied. The pulse became perceptible, the kidneys resumed secretion, the tremendous peripheral cyanosis was relieved, and in two days he was conscious. After fifteen days the patient was walking about the ward in tolerable comfort. No apparent change could be made out in the supposed aneurysm, but the polycythemia became much reduced, the pulse which had formerly presented extrasystoles, pulsus alternans, a jugular direct, and all manner of polygraphic curiosities became full and regular, though that on the right side remained small and at times imperceptible. Improvement was rapid during the summer months, so that the patient

was able to walk about the hospital grounds; but attempts to resume mercurial medication always met with early toxic symptoms, and the old intolerance for iodides was still present. Digitalis now acted splendidly, as did also other cardiac stimulants, so that the circulation was maintained at a very satisfactory level.

The Wassermann reaction remained strongly positive, and this fall, as he ceased to gain ground, and urinary suppression, with symptoms of cardiac failure, again supervened, it was determined to repeat the salvarsan, though some difficulty was experienced in inducing the operator to undertake the second treatment; 0.2 gram was finally given intravenously, and again collapse occurred, but after vigorous management, with final recovery. Again marked improvement in the cardiac action and in the general strength of the patient took place. He was able once more to get about the hospital, and again became a tolerably comfortable ambulatory patient. Through the courtesy of my colleague, Dr. Potter, into whose service he had now passed, I was permitted to examine him. Apparently at this time, October, 1912, the retrosternal dulness had somewhat decreased in breadth.

In late November he developed a gangrene of the great toe of the right foot, preceded by great pain in this foot and leg. A diagnosis of embolism from a detached cardiac or aneurysmal clot was ventured. Death soon followed.

Through the courtesy of Dr. Larkin I am permitted to abstract the following data from the detailed protocol:

The retrosternal mass was found to be a widely dilated but not much sacculated arch, which together with the entire artery was extensively diseased and ulcerated, though most of the ulcerations were clearly in a healing and not progressive state. The walls of the aorta also presented marked longitudinal striations and folds which Dr. Larkin interpreted to indicate that shrinkage or contraction of the vessel was in progress. The heart was greatly enlarged. It showed a diffuse interstitial myocarditis, with occasional small gummatous scars clearly now largely healed, and undergoing rapid fibrosis. The general arteries were markedly diseased, but the coronary vessels were not extensively involved, and, as in the aorta, little calcification was present, for the process appeared to be essentially one of fibrosis and fatty degeneration. The small pulse on the right was explained by an old thrombosis, with a subsequent canalization of the right brachial artery.

The liver was greatly enlarged, and showed the results of chronic congestion, diffuse connective-tissue hyperplasia, and quite frequent healed gummatous scars. The spleen was much indurated and enlarged, no gummas could be made out in it. The kidneys showed a diffuse fibrosis, with nodules of compensatory parenchymatous hyperplasia.

The striking features revealed by the necropsy were the evidences

of extensive disease of the aorta apparently undergoing healing and the presence of a syphilitic nephritis, hepatitis, and myocarditis, all well advanced in healing.

Realizing that microscopic study of these tissues might give a clue as to the manner with which healing may occur in the heart muscle in syphilitic myocarditis under the effects of salvarsan, such an examination was made. It seemed that this should be of special value, because in this case definite signs of improvement followed the use of the salvarsan, and little mercury or iodine was used. The changes therefore in such an instance would seem to be almost entirely due to the effects of the arsenic. The corroboration of the clinical benefit of treatment by direct anatomical evidence appears also to us of great importance.

MICROSCOPIC EXAMINATION. The muscle cells of the heart show in the main a considerable degree of atrophy, but with certain exceptions this atrophy appears to have been of pressure origin and not due to inherent disease of the muscle cells. For the greater part the striation is well preserved, a good many, however, show longitudinal striation, and there are many enlarged and karyokinetic nuclei, but cytoplasmic alterations are mostly wanting, except in the cells of the papillary muscles, where brown atrophy is quite general.

The connective-tissue interstitium is universally increased. This applies not only to the endomesium, but also to the connective tissue of the endocardium and epicardium. It is notably evident that hyperplastic connective tissue is most abundant and the evidences of recent growth most manifest about the arterioles of the coronary trunks.

Another peculiarity of this interstitial overgrowth is its highly cellular character, as though of rapid and rather recent formation. Cicatrization, or true scar formation, is not evident except in the papillary muscles and in the foci of old gummatous inflammation. Notwithstanding the fact that the connective tissue is so highly cellular, so apparently recently formed, few infiltrating leukocytes or wandering connective-tissue cells are present, and even about the blood channels which are crammed with red corpuscles few indications of active inflammation are to be made out. Lymphocytes are particularly few in number, both in the connective tissue and in the walls of the vessels, except again in the papillary muscles, where foci of infiltration and actively hyperplastic cells are present. Connective-tissue necrosis is also infrequent, but in the papillary muscles it is taking place, and degenerated foci of considerable size, marked by diffuse deposits of fatty and amorphous granules, are shown.

Notwithstanding the fact that the gross examination indicated that the coronary vessels were not markedly involved, the microscopic sections showed that the walls were much diseased. The

muscle coats are largely disrupted and replaced by necrotic and fatty material, the elastica is so broken as to be hardly discoverable, and the intima is much roughened and eroded. As a general thing, the caliber of the vessels is enlarged. A striking feature is the absence of evidences of active infiltration or inflammation in the walls, such as would be marked, for example, by foci of round-celled infiltration or by active changes about the vasavasorum. The veins show marked atheromatous changes, similar though in lesser degree to those shown in the walls of the coronary arterioles. The venules and capillaries are generally surcharged with red corpuscles.

The scars found at various points in the heart walls, alike of the auricles and ventricles, and apparently representing the sites of old gummas, show under the microscope a replacement process of the muscle by a growth of young areolar tissue like that found elsewhere in the specimens. This tissue is strangely free from infiltrating or wandering cells and from marked cicatricial formation, and notwithstanding the apparently recent nature of this connective tissue and the presence of hyperemic vessels the blood trunks and their vicinity are surprisingly free from evidences of inflammatory reaction. There is nothing anywhere evident indicating activity of process and nothing now to signify that it is a syphilitic process.

Sections through the aortic wall show extensive atheroma, mostly without calcification, although numerous and large atheromatous cysts are present, together with considerable areas of necrosis. Many of the vasavasorum are surrounded by foci of infiltrating round cells, but the process in the intima and the sub-endothelial coats is definitely one of degeneration and not now of proliferation and progress. Attached to the intima are found numerous masses of clot, more or less organized. The whole process is definitely in a stage of healing, except perhaps about the vasavasorum.

Spirochetes could not be demonstrated in any of these sections.

Sections of other viscera showed almost universally similar changes.

The microscopic picture, so far as the heart is concerned, may be summarized as a fibroid myocarditis, singularly free from evidences of inflammation or cicatrization, except in the papillary muscles, where the disease lesions were all found most marked. The changes in the muscle cells are clearly secondary to those in the interstitium. Even in those places where scar formation extends entirely through the heart walls, inflammatory and cicatricial alterations are strangely few. The disease process apparently originated about the coronary vessels.

The changes are most advanced in the papillary muscles, and in those foci where gummas have apparently existed.

The picture of the entire process is one of definite and rapid healing, and one which is apparently taking place with the minimum injury to the surrounding parenchymatous tissues.

In a small group of tertiary cases we have employed neo-salvarsan in place of the older arsenical preparation. So far as we can determine we have received quite as good immediate results as with the older preparation, but of course, sufficient time has not yet elapsed to judge accurately as to this fact nor indeed as to the permanency of improvement under salvarsan. In a physician with long-standing lues now under observation, after a long course of hypodermics of mercury salicylate, one dose of neo-salvarsan was injected intramuscularly, with a striking improvement in heart action and the disappearance of an apical systolic murmur which had decreased but not disappeared under the mercury.

As to the use of the iodides in syphilis of the heart. I do not believe from my somewhat limited experience in acute secondary syphilis that this drug has any appreciable effect, and I am much inclined to believe with Collins and others, that the iodides have little really antisiphilitic or specific action. On the other hand, in tertiary cases, and particularly in such as show persistent evidences of heart-muscle infiltration, I have found in not a few instances that the iodides apparently do what neither salvarsan nor mercury does. Where irregularities, dyspnea, and a certain degree of cardiac distress have persisted after the arsenical-mercurial treatment, in these cases great relief has apparently followed from the employment of the iodides. I am myself not inclined to consider this as due to a specific action of the iodides since I have seen equal apparent benefit in cases of probably non-luetic myocardial disease, with negative Wassermann, negative history, and negative findings so far as syphilis is concerned. I believe that the iodides in these cases favor absorption of degenerative or inflammatory products, and so favor restitution of normal cardiac action.

In several cases under our observation not only has there been a marked improvement in heart action, apparently amounting to cure, but in some instances, as cited also by Collins and Sachs, there has been actual disappearance of a definite aortic murmur, supposedly due to an aortic endocarditis. But why should we wonder at the restitution of a sclerosed or ulcerated heart valve under syphilitic medication when we take as a matter of course the absorption of a gumma of the liver or brain under the same general treatment?

In a recent report before the Internal Section of the New York Academy of Medicine, Longcope records striking results from the arsenical treatment of syphilitic aortitis even in long-standing and advanced cases. Doubtless in Longcope's series of syphilitic aortitis many if not all his cases were complicated by myocardial lesions, and no doubt part of the benefit achieved in his aortic

cases was due to betterment of myocardial lesions, just as beyond question some of the symptoms of my cases of syphilitic cardiac disease have been in part relieved through the effects of the drug on the aorta, there is no possible differentiation, of course, when it comes to judging the effects of treatment in either instance.

Adjuvant treatment, as though the cardiac lesions were not specific but idiopathic or general, is, of course, indicated. A few of my cases have taken the Nauheim treatment at home or in Nauheim with apparent benefit. Practically all of them have had digitalis or strophanthus at times as indicated. It goes without saying that all these circulatory measures should be employed as in other types of heart disorder, but the point which I wish to bring out in this paper and to emphatically emphasize is that they are secondary and relatively unimportant—the great essential is to treat these syphilitic lesions as syphilis.

As to the manner in which antisypilitic medication cures or relieves lesions of the heart in syphilis, I have as yet little direct absolute evidence to offer, nor is it likely that I shall be able in the future to secure much material of conclusive character in this regard. The case just reported is perhaps as direct as can be expected. Inasmuch as I believe that I have demonstrated from previous studies that the characteristic and most important lesion in cardiac involvement is a gummatous process or an infiltration, a true syphilitic myocarditis, it seems logical to assume that benefit can be reached only by the local death of the spirochetes and by the subsequent absorption of the exudate and foreign tissue laid down in the myocardium as a result of the syphilitic infection. If, as seems indicated by the case just reported, this does take place, then it is easy to understand how improvement in heart action follows so promptly as we have found in many but not all the patients under our observation.

I have purposely made only a few references to the literature of the subject, but have confined myself to the data which I have collected and on which I have based my personal conclusions.

CONCLUSIONS. 1. Serious involvement of the heart is frequent in syphilis. Epicardium, endocardium, or myocardium or all together may be so diseased.

2. Cardiac involvement may develop early in the infection, though its symptoms may not be apparent until late.

3. The signs and symptoms are those of cardiac disorder, and little or nothing except the history, general aspects, and the Wassermann reaction may indicate the true etiology.

4. Treatment should be first along indicated circulatory lines, secondary as to time, but most productive and important of all it must be specific.

5. Good results, cures in many instances, will follow appropriate antisypilitic treatment.

6. The special method of treatment should be individual, but both mercury and salvarsan are efficacious in the condition; usually they are preferably combined, in some instances the former, in others the latter acts best. Iodine is an efficient adjuvant in at least some instances.

7. Treatment should be continued until a permanent negative Wassermann is attained. Subsequent to this the management of the case should be along circulatory, not luetic lines.

SYPHILIS IN THE ETIOLOGY OF FIBROUS OSTEITIS.¹

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ASIDE from the acute and chronic bacterial infections, tuberculosis and neoplasms of bone, there is a group of bone diseases of which leontiasis ossea, osteitis deformans, and osteomalacia are examples, whose stumbling nomenclature almost cries out for the light of etiology. It is for the purpose of suggesting the etiologic relationship between one of this group, osteitis fibrosa, or better, as termed by Bloodgood, chronic osteomyelitis fibrosa solida, and tardy hereditary syphilis that this communication is presented. The most recent contribution on this subject is by Elmslie² who states: "Beyond the opinion that fibrous osteitis is an inflammatory lesion, we must at present acknowledge that we know nothing of its pathology." In an exhaustive communication on this and kindred affections Bloodgood³ says: "I, therefore, have been unable to find any definite etiologic factor, and I cannot agree with those who look upon the lesion as the result of trauma. . . . I agree with all the more recent investigators that the disease is an inflammatory one, in which the medullary tissue is replaced by a new formation of connective tissue with or without cyst formation." After reciting the history of my case, I shall endeavor to establish the premises upon which I conclude that this, if not many other similar cases, is due to syphilis of the late hereditary form.

CASE I.—X. Y., male, farmer, aged twenty-two years, was referred to me in the Surgical Out-patient Department of the University Hospital by Dr. Charles C. Wolferth, of Clarksboro, N. J., January 2, 1912. His chief complaint was left-sided limp.

¹ Read before the Pathological Society of Philadelphia, January 24, 1913.

² British Med. Jour., November 16, 1912, p. 1367.

³ Annals of Surgery, 1910, lii, No. 2, 145.

He had enjoyed (and still enjoys) perfect health until about seven years ago, when aged sixteen years, when he was thrown off a horse, landing on the left hip—not a severe fall, however. He was treated for fracture of the femur for eight weeks by Buck's extension, and used crutches five or six weeks after that time. He was then able to get around without any assistance. After that he had pains every winter on walking; no pain when not moving the leg. Two years before the fracture when aged fourteen years he noticed pain, and on examining his leg found the thigh swollen and bowed—this being the first knowledge of his condition. The swelling was larger after than before the fracture. The leg was bowed before the fracture, but was not as short as it is now.

His family history was directly negative, but indirectly suggestive.

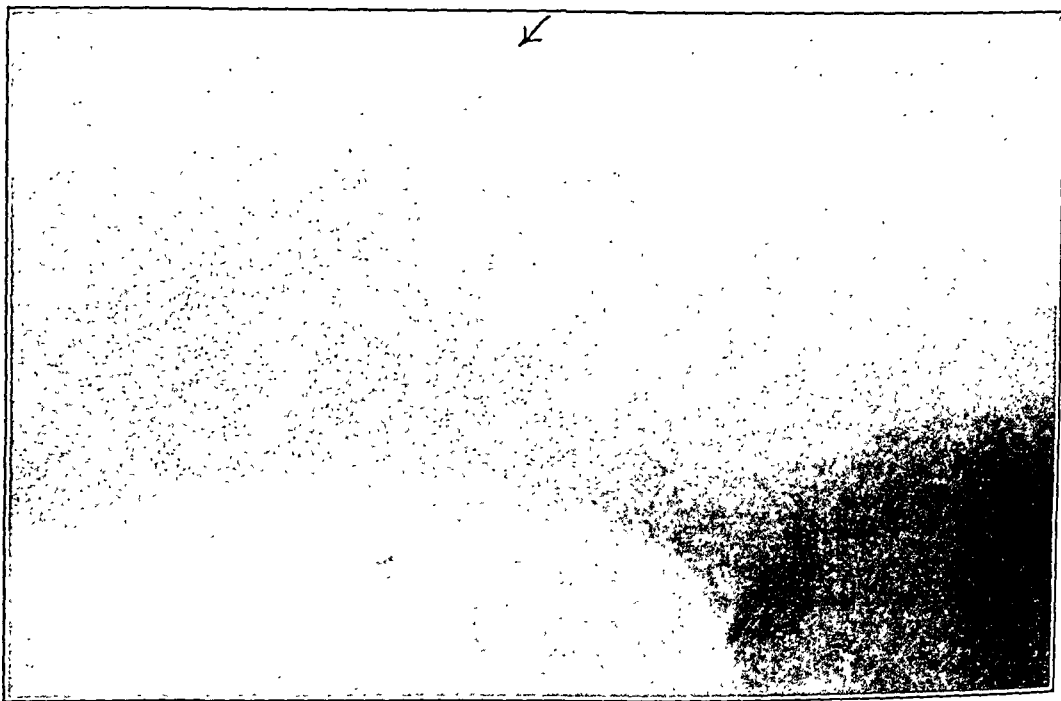


FIG. 1.—Syphilitic osteitis fibrosa of femur. Note thickening and roughness of surfaces, obliteration of medullary cavity, alternating areas of bone production and bone absorption, and line of pathological fracture.

Examination revealed the excellent general health and condition of a normal country lad. The left thigh was markedly bowed, with outward convexity (Fig. 1), and the femur was thickened, roughened, but not tender. There were no sinuses. Measurements taken from the internal condyle of the femur to the anterior superior spine of the ilium showed: Right leg, $18\frac{3}{4}$ inches; left leg, $16\frac{1}{4}$ inches, therefore $2\frac{1}{2}$ inches of shortening. None of this shortening was contributed by the femoral neck, as measurements from the top of the great trochanter to the symphysis pubis showed,

although there was apparent shortening here, due to the great bowing. The point of greatest convexity was opposite the termination of a straight line drawn from the anterior superior spine $5\frac{1}{2}$ inches downward.

The absolute passiveness and quiescence of the lesion, and the length of time during which it had existed without producing either the sinuses of tuberculosis or the cachexia of malignancy, at once suggested syphilis of the late hereditary form. After a few days the Wassermann reaction returned positive, and the skiagram (Fig. 1) revealed great increase in diameter of the upper half of the femoral shaft, with interruption of the medullary cavity and contiguous areas of bone production and bone absorption, with a clear and incomplete line at the point of greatest convexity, which indicated the site of the pathological fracture.

The patient was immediately put upon corrosive sublimate and iodide of soda and with the help of Dr. De Forest Willard an ambulatory brace was devised which transferred the weight from the left lower extremity from the pelvis to the ground.

During the eleven months that have elapsed since then (January 2, 1912) until the present time (December 2, 1912) the mixed treatment was maintained, neosalvarsan administered twice weekly, and the course of the disease studied by frequent skiagrams and blood examinations. During this time the patient maintained the best of health, and locomotion was considerably facilitated by the brace. Pains have disappeared gradually under brace and treatment.⁴ Has very slight pain now, but none when resting.

On December 2, 1912, the Wassermann continuing negative and the latest skiagram (Fig. 2) showing more homogeneity of the texture of the bone, with complete healing of the line of fracture, it was thought the time had arrived for correction of the deformity by osteotomy and curetting of the area. In the meantime the correlation between this pathologic picture and that presented by osteitis fibrosa had impressed itself more firmly upon the writer.

This picture corresponds to syphilis, in that the essential lesions were those of formative rather than destructive periostitis, osteitis (which here was rarefying, predisposing to fracture), and osteomyelitis, and to syphilis of the late hereditary type in that it appeared at about puberty. The Wassermann reaction also was positive. So, too, it corresponds to osteitis fibrosa in its age of onset, the insidiousness of the process in the medullary cavity—the pathologic fracture after slight trauma being the first sign,

⁴ D'Arcy Power (British Med. Jour., December 7, 1912, p. 1603) states: "We have found that the pain of periostitis and of osteitis in patients who have congenital or acquired syphilis is markedly improved" (under treatment by salvarsan).

A CASE OF STRYCHNINE POISONING.

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J. B., aged forty-nine years, was admitted to the University Hospital on November 14, 1911, suffering from chronic lymphatic leukemia. He was a large, powerful man, weighing 190 pounds stripped. On December 5, at 8.15 A.M., he received through error 15 grains of strychnine sulphate in three capsules. At 9.15 A.M. I was sent for hurriedly. The patient was found rigidly extended on his bed, conscious, and extremely apprehensive that some terrible thing was about to befall him. He complained of intense pain in the back of the neck. From time to time his muscular rigidity increased suddenly, and he repeatedly asked to be held on the bed for fear that he should throw himself off. He was immediately given a quarter of a grain of morphine and preparations were made to wash out the stomach. A few minutes later, on attempting to pass the tube, it was found that the patient could not separate his teeth by more than half an inch. The trismus rapidly increased, the jaws became rigidly shut, and the patient passed into a severe tonic convulsion with cessation of respiration. During this he became intensely cyanotic, the pulse was very small, rather rapid, high tension, and with frequent intermissions, apparently due to the occurrence of extrasystoles. A probable diagnosis of strychnine poisoning was made at this time. Efforts made to open the mouth with a gag during the convulsion were unavailing, and resulted in loosening several teeth. One-tenth grain of apomorphine was injected. Shortly after, the stomach tube was successfully passed through a nostril and the stomach thoroughly washed out. The patient vomited repeatedly during this washing and the vomitus contained milk curds. The washing was repeated at 9.50 A.M., 10.20 A.M. and 11.00 A.M., and on each occasion there was vomiting. A second severe general convulsion occurred at 10.00 A.M. Shortly after this chloroform anesthesia was started. This was changed to ether at about 11.00 A.M., and the patient was kept continuously under the anesthetic until 4.30 P.M. An enema containing forty grains of sodium bromide and twenty grains of chloral hydrate was given at 10.30 A.M. No further severe general convulsions occurred but milder convulsive movements were noted at 11.00, 11.30 A.M., 12.00 M., and 12.25, 12.40 and 12.50 P.M. Other milder convulsive movements were not recorded. These mild convulsions were frequently precipitated by the patient's efforts to talk, by attempts to move him, by noises, etc. They occurred especially when the anesthesia became lighter. They consisted of momentary periods

of extreme stiffening of the trunk and extremities, and they were usually accompanied by involuntary cries and expressions of pain. They did not produce cyanosis. As it was felt that an indefinite quantity of the strychnine might have passed into the intestines, two drops of croton oil were placed on the tongue at 9.40 A.M., and this dose was repeated at 12.45 and 3.00 P.M. No bowel movement, however, occurred until evening; 123 c.c. of urine were obtained by catheter at 1.30 P.M. and 390 c.c. at 6.25 P.M. Thereafter micturition was voluntary. At 5.45 P.M. a pint of saline solution, with 10 grains of diuretin, was given by rectum, and this was repeated about once in two hours until noon of the following day. A flood of urine and numerous small stools were passed during the night. Repeated twitchings of the muscles were noted up to midnight. On the following morning the patient complained of soreness of the muscles, which persisted for several days. For several nights he was restless, and complained of muscular twitchings. On December 10 he developed a severe stomatitis, which lasted about ten days. No definite cause for this could be found, but it was supposed to be due either to an infection following the injury to his teeth or to the local irritant effect of the croton oil. He left the hospital on January 1, 1912, with no evident remaining effect of his experience.

This case is noteworthy because of the amount of strychnine taken (15 grains). The fatal dose is commonly stated to be $\frac{1}{2}$ to $1\frac{1}{2}$ grains, although according to Gadamer it is considerably higher (2 to 6 grains¹). Over $1\frac{2}{3}$ grains were recovered from the urine of our patient. Much larger doses taken by the mouth have of course been recovered from under prompt treatment; even from such exceptional doses as 75 grains, 60 grains, and 20 grains. The dose taken by our patient stands among the large ones on record. His recovery was due in part to the presence of food in the stomach, which retarded the passage of the poison into the intestines and in part to the prompt emptying of the stomach at the onset of symptoms; $4\frac{1}{2}$ grains were obtained from the first stomach washings, but unfortunately, the later washings were not analyzed.

The case is interesting on account of the attempt to determine quantitatively the amount of strychnine excreted in the urine and the rate of excretion. Examination of the urine of fatal cases of poisoning have usually shown only minimal amounts and frequently none at all (Masing and Dragendorff²). Lesser³ found traces in only 2 of 5 fatal cases. Kratter⁴ found it in the urine of

¹ The literature of strychnine poisoning has been carefully summarized by E. Rapmund, *Vierteljahrschr. f. gerichtl. Med.*, 1911, xlii, 243; E. Allard, *Vierteljahrschr. f. gerichtl. Med.*, 1903, xxv, Suppl. 234; R. Kobert, *Lehrbuch der Intoxikationen*, Zweite Auf., 1906, 1153.

² Quoted in Allard, loc. cit., 299.

³ *Wien. med. Woch.*, 1882, xxxii, p. 214.

⁴ *Vierteljahrschr. f. gerichtl. Med.*, 1898, xv, 269.

a man who died in one and a half hours. On the other hand medicinal doses of this drug appear promptly in the urine. Mann found it in thirty minutes,⁵ Kratter in thirty-five minutes, Rautenfeld in two hours, and Hale⁶ in two to three hours. The excretion continues for one⁷ to four days,⁸ or possibly longer. In animals it may appear very promptly in the urine. Ipsen⁹ found it in two and one-half minutes in rabbits and five minutes in dogs. Rapmund¹⁰ found it in four minutes in rabbits.

The specimens of urine from our patient were carefully saved and sent to the hygienic laboratory of the University of Michigan, where the analyses were made under the direction of Dr. V. C. Vaughan. From each specimen 100 c.c. of urine were evaporated to dryness on the water-bath. The residue was extracted with 100 c.c. of alcohol and again evaporated to dryness on the water bath. This residue was dissolved in 100 c.c. of water. It was then made feebly alkaline with ammonia and shaken in a separating funnel with 100 c.c. of chloroform. The chloroform was evaporated to dryness and the residue was again taken up in slightly acidulated water, again made alkaline with ammonia, and again shaken out with chloroform. The residue from this last chloroform extraction was rubbed up with a few drops of concentrated sulphuric acid and heated for one-half hour on the water bath. It was again dissolved in water, to which ammonia was again added, until the solution was slightly alkaline. It was then shaken out with chloroform, the chloroform was evaporated to dryness, and the residue weighed.

The results of the analyses of the urine of our patient are shown in the following chart. Unfortunately no analyses were made of the urine which was passed between 6.05 A.M. on December 6 and that which was passed at 2.30 P.M. on December 7.

ANALYSES OF URINE AFTER TAKING 1.0 GRAM STRYCHNINE AT 8.15 A.M.
ON DECEMBER 5, 1911.

Time passed.	Amount of urine in c.c.	Specific gravity.	Albumin.	Strychnine in grams.	Average per hour.	
					Amount urine.	Strychnine.
December 5, 1.30 P.M. . .	123	0.0010	23	0.0002
6.25 P.M. . .	290	1.001	Positive	0.0200	58	0.0040
11.30 P.M. . .	500	1.010	0.0490	100	0.0098
December 6, 1.15 A.M. . .	350	1.009	0.0105	200	0.0060
2.55 A.M. . .	220	1.007	0.0110	120	0.0060
3.45 A.M. . .	185	1.009	0.0027	200	0.0032
6.05 A.M. . .	300	1.009	0.0019	125	0.0007
December 7, 2.30 P.M. . .	290	Trace		
December 8, 24-hour specimen		Faint trace		
December 9, 24-hour specimen		None		

⁵ Wien. med. Woch., 1882, xxxii, p. 214.

⁷ Kratter, loc. cit.

⁹ Vierteljahrschr. f. gerichtl. Med., 1892, iv, 15.

⁶ Jour. Phar. and Exp. Therap., 1909, i, 39.

⁸ Hale, loc. cit.

¹⁰ Loc. cit.

During the earlier stages of the poisoning the amount of urine was diminished. When catheterized at 1.30 P.M., 123 c.c. were obtained, and we have no knowledge as to how much of this may have been excreted previous to the onset of the poisoning. At best not more than 23 c.c. per hour were excreted during this period, and it seems probable that very little urine was formed during the acute symptoms. According to Grützner¹¹ the constriction of the renal vessels during strychnine poisoning inhibits the flow of urine despite the increased blood pressure. The marked increase in the second portion of urine (58 c.c. per hour) was due mainly to the improved renal circulation, for the salt solution enema given forty minutes before this urine was obtained could hardly have been solely accountable for the considerable quantity of urine. The subsequent flood of urine was evidently due in part to the enemata and in part to the improved renal circulation.

During the acute stages of the poisoning very little strychnine was excreted, only 1 milligram having been obtained from the urine passed at 1.30 P.M. Had the patient died within two hours still smaller amounts, probably only traces, would have been recovered from the urine.

Following this period the excretion of strychnine increased rapidly, the maximum being reached between the hours of 6.25 P.M. and 11.30 P.M. during which period 49 milligrams were excreted, an average of almost 1 milligram per hour. The amount excreted diminished rapidly toward morning, the rate between 3.45 A.M. and 6.05 A.M. being less than 0.1 milligram per hour. During the second day no analyses were made. On the third day a distinct trace was obtained, and on the fourth a faint trace. On the fifth day no strychnine was obtained. Altogether, about 96 milligrams ($1\frac{3}{5}$ grains) were recovered from the urine. The analyses are noteworthy in showing (1) how little strychnine was excreted during the most acute stage of the poisoning, (2) that the major amount was excreted within twenty-four hours, and (3) that the excretion was not completed for three or four days.

But few observations on the effect of strychnine poisoning upon the body temperature of man are available. Observations on animals by Harnack,¹² Harnack and Hochheim,¹³ Högyes,¹⁴ Kionka,¹⁵ and Rapmund,¹⁶ indicate that, as a rule, the temperature rises during the convulsions and tends to fall between them. Indeed, in some instances the fall has predominated and the temperature was lowered throughout. Rapmund¹⁷ records a rise from 39.1° to 42° C. on one dog, and several similarly large rises are on

¹¹ Arch. f. Physiol., 1875, xi, 385.

¹² Zeitschr. f. klin. Med., 1894, xxv, 16.

¹³ Arch. f. exp. Path. u. Phar., 1881, xiv, 113.

¹⁴ Abstract in Fortschr. d. Med., 1898, xvi, 941.

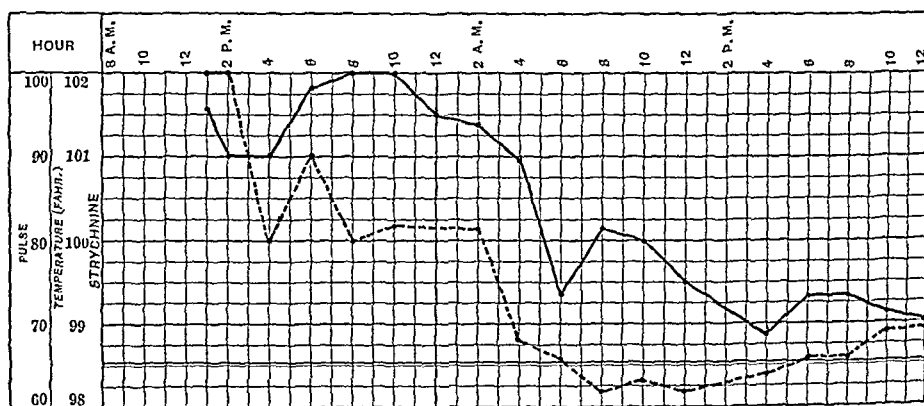
¹⁵ Loc. cit.

¹⁶ Arch. exp. Path. u. Phar., 1903, xlix, 157.

¹⁷ Loc. cit.

record.¹⁸ Experiments by Kionka and by Harnack indicate that both the heat production and the heat elimination are increased, the resulting body temperature depending upon which of the two predominates. Harnack found that doses of strychnine which produced no convulsions might increase the heat production.

One hesitates to transfer these results to man, both because of the varying results obtained on animals and because of the finer temperature adjustment in man. Only occasional observations have been made upon the body temperature in cases of human poisoning with strychnine. Barthélemy¹⁹ and Lesser²⁰ record normal temperatures. Habel's²¹ patient, who took about 0.18 gram at 8.00 A.M., showed an evening temperature of 38° C., with subnormal temperatures on the following days. Honigmann's²² patient showed a temperature of 38.1° C. twenty hours after taking the poison, and for several days his temperature ranged 38° and 38.4° C. (100.4° to 101.1° F.). He had an acute nephritis. In Ott's²³ patient the temperature rose to 101° F. on the first and second days, subsiding on the third day with rapid and complete convalescence. Wood states that he has never seen a temperature chart which showed fever after strychnine poisoning, nor have I been able to find a complete chart. The following chart



Temperature showing in continuous line; pulse in broken line. For the week previous the temperature had been 97.8° to 98.6° F., pulse 61 to 94.

is therefore of interest, since it shows a definite elevation of temperature for over twenty-four hours after taking the poisonous dose of the drug. Rectal temperatures were taken every two hours from 1.00 P.M. on the day of the poisoning to 4.00 A.M. on the following day, after which the temperature was taken in the axilla or by the mouth. These records show a marked and continued elevation of temperature, the highest being 102° F. It is

¹⁸ Högyes, Loc. cit.

²⁰ Loc. cit.

²² Deut. med. Woch., 1889, xv, 435.

¹⁹ Ann. Hyg., 1885, xiii, 130.

²¹ Münch. med. Woch., 1898, xlv, 7.

²³ Med. News, 1894, ii, 270.

noteworthy that all of these temperatures were taken after the severe convulsive stage had passed.

In animals both heat production and heat elimination are increased. One may judge the heat elimination in man roughly by the warmth of the extremities, the presence of perspiration, and the size of the peripheral pulse. During the early convulsive stage of the poisoning our patient had a very small radial pulse and the extremities were cool; but throughout the latter part of the first day the skin was warm and was covered with a moderate perspiration, while the radial pulse was unusually large; all of which characters we have learned to associate with a rapid rate of blood flow through the arm. Apparently, therefore, the body was eliminating heat in excessive quantities after the convulsive stage was over, and since its temperature remained elevated, it seems probable that the heat production was also markedly increased. When, however, we consider the fine adjustment of heat regulation in the normal individual and the rapidity with which any excessive heat produced in the body is eliminated, it is surprising that the elevation of temperature should have persisted for over twenty-four hours in our case, for two days in Ott's case, and for several days in Honigmann's case. One can hardly avoid the conclusion that strychnine poisoning may disturb the fine adjustment of heat regulation in the body, and that in a certain sense, we have a condition analogous to that which prevails in fever.

In conclusion I wish to thank Dr. V. C. Vaughan for his valuable suggestions and for the analyses which have made the case one of unusual interest.

INSUFFICIENCY OF THE PULMONARY VALVE.

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A STUDENT who wishes to investigate this subject will find himself indebted especially to four writers, Barié, Gerhardt, Gibson, and Pitt, and most of all to the first mentioned.

Barié¹ in the historical introduction to his paper reproduces a case reported by Morgagni² which is of great interest: "The patient was a young girl, sick and bedridden since birth, affected with persistent dyspnea and lividity of the skin. She died when sixteen years old. At the autopsy the right ventricle was found dilated, the pulmonary valves were cartilaginous, and so united as scarcely

¹ Arch. gén. de méd., 1891.

² De Sedibus et Caus. Morborum, epist. 17, chap. 12, t. i, p. 359, trad. Destonnet, 1837.

to leave an orifice as big as a lentil for the blood to pass through. But in addition to this orifice there were some small membranous fleshy growths placed in such a manner as to fulfil the function of a valve in permitting the blood to pass out, acting as an obstacle to blood that might regurgitate."

Barié's study of insufficiency of the pulmonary valve is based upon 58 cases; in 43 of them there were autopsies which justified the diagnosis; in 8 the observations were exclusively clinical, while 7 were obtained from references in the literature.

In speaking of the pathologic anatomy, Barié refers to the fact that there may be variations in the number of the valves. There may be two or four or five instead of the customary three. Grawitz reports an interesting case in which a leaflet occupied the anterior and posterior thirds of the lumen of the artery, while the middle third had none. There was no trace of endocarditis. In my first case, to be reported later, there were four leaflets. In a case reported by Kolisko there were also four valves, "but the posterior was much smaller than the other three."

Often a difference in the number of valves is associated with malformations, such as communication between the ventricles, as in cases reported by Lambl and Litten. The valves themselves may be defective through atrophy, shortening, or deformity. Barié refers to a curious case which he saw at autopsy in which a baby, aged three and a half months, had two normal leaflets, but the third was small and rudimentary, permitting regurgitation.

Bouillard reports a case in which the pulmonary artery was guarded by a horizontal partition pierced at its centre by a perfectly circular opening 0.006 mm. in diameter. This sort of hymen presented upon its convexity three small folds or loops. Though this patient suffered from infancy with extreme dyspnea and cyanosis of the face, and had, moreover, a persistent foramen of Botal, she died at an advanced age.

The valves may be fenestrated. In such cases they are supposed to be unduly thin, permitting partial rupture and even some small loss of valve substance. Several interesting cases have been reported.

Endocarditis of the valves is another cause of insufficiency. It may lead to complete destruction of one or more leaflets. The valves also may be thickened; retracted and of almost cartilaginous hardness by a chronic proliferating process, or, on the other hand, they may be covered with vegetations.

Rarely aneurysm of the valves is found. Barié has found 3 cases. Ulcerative lesions also occur and may result in perforation, as indeed may aneurysm, and occasionally in destruction of one or more leaflets.

Rupture of the valves, while a rare accident, has been encountered by Bernhardt, Wahl, and Chevers.

LESIONS OF THE PULMONARY ARTERY. Insufficiency of the pulmonary valve may be due to narrowing of the pulmonary orifice. Out of 43 cases examined by Barié, 23 showed stenosis and insufficiency. In 9 there was dilatation of the artery, due partly to the distending force of the systole of the right ventricle and partly to disease of the artery itself.

Atheroma of the pulmonary artery has been found in a small number of cases by Chevers, Wilks, Benedict, and Bristowe.

As to the frequency of the lesion, C. Gerhardt³ quotes Weckerle:⁴ In 846 Munich cases the right heart alone was involved in 3.9 per cent.; in 1.54 per cent. the pulmonary artery in general and in 0.59 per cent. the pulmonary valve alone was affected. Willigk in 4547 dead bodies found inflammation of the pulmonary valve 9 times; twice this valve alone was involved.

C. Gerhardt has assembled 29 cases, with autopsies. Although inflammation of the valve is given as the cause in three-fourths, rheumatic fever is recognized positively as the cause in only 7; 1 only is assigned to gonorrhea, whereas in 60 grouped by Pitt as infective, gonorrhea was put down as the cause in 8.

The age in Gerhardt's cases varied remarkably, the youngest being eleven and the oldest aged eighty-four years; nearly one-third died in the fourth decade and one-third died in the second and third decades.

INCOMPETENCE OF THE PULMONARY VALVE. Dr. G. Newton Pitt,⁵ says that this is the rarest of valvular lesions of the heart, only 24 cases having been noted in the postmortem room at Guy's Hospital out of 16,000 examinations during a period of thirty-two years. Pitt has added 51 to those already reported (39 being unpublished cases from the records of Guy's Hospital), making a total 109, besides 30 published clinical cases which were not verified after death.

As to etiology, 60 are classified as infective endocarditis, 18 due to dilated pulmonary artery, 14 to aortic aneurysm pressing on the pulmonary valve, 13 to abnormality in number of valves, 14 to pulmonary stenosis, while 6 are unclassified. The recorded ages in the 60 infective cases show that the lesion is most frequent between the ages of twenty-one and thirty, but is nearly as frequent from eleven to twenty years, (13 cases) and from thirty-one to forty years (12 cases). At other ages it is rare.

No obvious cause was found in 21; a patent ventricular septum in 10; congenital pulmonary stenosis in 8; patent ductus arteriosus in 3; gonorrhea in 8; puerperal infection in 5; pyemia in 4; pneumonia in 5 cases.

All four valves were affected in 4 cases; hemoptysis and dyspnea

³ Charité Annalen, 1882, xvii, 255.

⁴ Ueber Uiceröse Endocarditis der Pulmonalkappen., Münch. med. Woch., 1886.

⁵ Allbutt's System of Medicine, 1909, vi, 310.

were the symptoms chiefly noticed. In 8 the implication of the pulmonary valve was definitely diagnosticated. In 5 only a systolic bruit appears to have been observed. In 3 it is definitely stated that no bruits could be heard. In others both a diastolic and a systolic bruit were noted.

In 5000 autopsies mitral stenosis was present in 19 out of 21 in which dilatation of the pulmonary artery was noted, and is consequently the chief lesion to be considered. It was the dominant lesion in both of my cases. Graham Steel, G. A. Gibson, Sir J. Barr, and Sir Dyce Duckworth have published over 20 postmortems secondary to mitral stenosis. There were 3 more cases at Guy's between 1901 and 1906.

Dilg has collected the cases showing abnormal number of cusps: Two pulmonary valves, 64; four pulmonary valves, 24; five pulmonary cusps, 2.

Pulmonary stenosis (14 cases): In 8 there was ulcerative endocarditis; in 2 a dilated pulmonary artery; and 1 only two cusps. In 3 a diastolic murmur was heard in spite of a congenitally stenosed pulmonary orifice.

Pitt calls attention to the remarkable fact that in cases of the most extreme mitral stenosis in which a similar defect is ultimately set up in the tricuspid valve the pulmonary cusps invariably escape and do not show even a trace of thickening. The influence of rheumatism as a cause is far less in the pulmonary than in any other valve.

The free margins of the cusps were more or less adherent in 18 and retroverted in 4 cases.

The statement usually made that pulmonary incompetence is a congenital defect is not accurate. About one-quarter of the collected cases showed evidence of old pulmonary stenosis, and in the same proportion there was some abnormality in the number of the valves. There is practically no evidence that trauma is a cause of incompetence.

CLINICAL SYMPTOMS OF PULMONARY INCOMPETENCE. In regard to the symptoms and clinical course, Pitt says that it is possible to make two groups, one in which the course is rapid, sometimes with no definite symptoms pointing to the heart, more frequently with signs of a general infective process, such as puerperal septicemia, in which the heart may be discovered to be involved. In these cases in more than one-half the number in recent years a correct diagnosis has been made.

The second group comprises much the larger number. There are definite cardiac symptoms, such as dyspnea, cough, edema of the lower limbs, etc., and a careful study of the physical signs will in most instances enable one to discover the lesion. It must be admitted, however, that where there are multiple lesions, especially aortic insufficiency, as in both of my cases, the diagnosis requires

some courage, not to say boldness, as well as skill. The most important considerations in the diagnosis are:

1. The size of the right ventricle: The cardiac dulness is increased in width, the apex beat is displaced to the left, but not downward, except of course in combined lesions. In some cases pulsation can be detected in the second or third left intercostal spaces, a pulsation supposed to be due to the infundibulum of the right ventricle.

2. Thrills are sometimes felt: They may be systolic or diastolic in time, the former indicating stenosis of the pulmonary valve.

3. A positive jugular pulse has been noted in some cases.

4. The most important sign is a diastolic murmur, with maximum intensity along the left border of the sternum in the second intercostal space. It is conveyed down the sternum toward the fourth interspace. Exceptionally it may be heard near the apex of the heart, or even in the epigastrium; when very loud it has been heard in the interscapular region. The quality varies widely. Some writers (especially Gerhardt) speak of it as rougher than the aortic diastolic murmur but I do not believe this is so frequent as to be of value in diagnosis. It could not be determined in either of my cases.

The pulse is soft and regular. Subjective symptoms are chiefly those referred to the lungs; as dyspnea, cyanosis, cough, spitting of blood from congestion, or infarct.

Bamberger has described a pulsation of the border of the right ventricle between the ensiform cartilage and the seventh right costal cartilage, and says that pressure of the finger here detects a thrill. Gerhardt has demonstrated it twice. The diastolic murmur is said by Bernhardt, to be stronger in expiration.

Gerhardt thinks we should be able to hear a double sound in the arteries of the lung in pulmonary insufficiency analogous to that heard in the arteries of the trunk in aortic insufficiency. He has heard it five times, but in only one case was pulmonary insufficiency established by autopsy. He says the sounds are best heard farthest from the heart, at the outer border of the right shoulder-blade. He describes, further, "an audible capillary pulse of the small circulation," which he has heard in three cases. It consists in an increased intensity of the vesicular breath sounds during systole. In his cases the sound was heard two to four times during a slow inspiration.

Gerhardt also gives tracings of the air pressure in the bronchi and trachea obtained by introducing a tube connected with a manometer into one nostril; the breath is first drawn in, and then held and then breathed out through the other nostril. The curve in pulmonary insufficiency resembles an exaggerated radial sphygmogram in aortic insufficiency.

CASE I.—The first patient was a boy admitted to the Philadelphia General Hospital in March, 1910, with extreme dyspnea

and anasarca, said to be of four months' duration. His father and mother were living and well. The patient was one of thirteen children, eight surviving, the oldest aged twenty years, the youngest one month.

The boy had had mumps, diphtheria, and smallpox when quite young; his first attack of rheumatism had occurred when five years of age, since which time there had been several attacks. Scarlet fever occurred two years before his admission to the hospital.

While the boy was fifteen years old at the time of his death, he was not more mature in mind or developed in body than a boy aged ten years. He was small of stature, and there was no development of hair upon his body. Following his first attack of rheumatic fever when he was five years old, he was dyspneic on exertion, so that he could not run and play with other children.

In 1909 he was taken to the Mary J. Drexel Home because dyspnea was so great as to compel him to stay in bed. From that time to his death he was bedridden most of the time. After prolonged rest in bed, sometimes with the relief afforded by the withdrawal of ascitic fluid from the abdomen, he would recover sufficiently to be in a wheeled chair, or even to go home; but he would soon return, with an increase in dyspnea, more cough, inability to lie down or to sleep, and more or less cyanotic. Much of the time his condition was truly pitiable.

After tapping on October 5, 1911 pulsation of the liver was distinctly visible beneath the costal margin, projecting from it to the right of the epigastrium, and pointing toward the umbilicus was a prominent mass about the size of a small orange, which was soft fluctuating, and painless. Pressing in deeply one could feel a hard nodule about the size of a hickory-nut, which was also free from tenderness. The enlargement was looked upon as a distended gall-bladder, the hard nodule as a stone. The fluctuating swelling above described did not fully reach down to the lower border of the right lobe of the liver; it was possible therefore that it was the gall-bladder which was kept from reaching the lower border by adhesions, or that it was a much softened fluctuating gumma. The latter was rendered possible by the existence of an aortic insufficiency which had developed since the previous admission of the patient in 1910, and by the detection of a positive Wassermann reaction. There was also over the left lobe of the liver a flattened oval elevation about three inches in transverse and two inches in vertical diameter.

October 17. One gallon of turbid yellowish fluid was withdrawn from the abdomen. Following the last tapping the swelling in the region of the gall-bladder was less distinct and that in the region of the left lobe more so.

October 18. The apex beat at present is in the sixth interspace, midaxillary line, six and one-eighth inches from the tip of the

xiphoid. The right border of the heart is two finger breadths to the right of the sternum in the fourth and fifth interspaces. Pulsation is visible over the abdomen and the chest. Both right and left lobes of the liver pulsate strongly. There is a faint presystolic thrill at the apex; no thrill is felt at the other orifices. At the apex there is a pronounced thumping systolic sound followed by a high-pitched whistling murmur. As one approaches the sternum from the apex the systolic murmur becomes more rough, blowing, and louder, and a diastolic sound is heard, succeeded by a diastolic murmur; the systolic murmur is louder over the third right rib, and here also a loud diastolic murmur is heard, not as loud as the systolic. To the right of the xiphoid there is a coarse, rough, low pitched systolic murmur. There is some preservation of the systolic sound. There is a distinct pulsation of the vessels of the neck, the jugulars, and the liver.

Liver: Lower border of the right lobe reaches to the upper border of the transverse umbilical line. In the midaxillary line it is thick, not tender, and pulsates strongly, projecting a little farther down than the rest of the liver, and apparently separated to the left by a groove or notch. Beyond this notch toward the umbilicus there is a projecting, somewhat elastic, not tender mass, intimately connected with the liver. Still further to the left and higher up, four and one half inches in a diagonal line from tip of the xiphoid, there is a hard nodule the size of a marble. Below that and a little to the left about one and a half inches is another nodule which is a little smaller. The latter nodule is apparently at the extreme lower border of the liver. About two inches to the left of the xiphoid, beginning a half inch below the margin of the ribs and extending down two inches, is a prominent oval swelling on the surface of the liver, two inches in vertical and three inches in transverse dimensions. The abdomen is as it has been, distended with fluid, the flanks bulging, the veins in lateral walls distended, and the navel projecting.

The pulse is of the Corrigan type. Capillary pulsation shows faintly in the forehead, but not in the lips.

October 1. Urine: Straw color; light flocculent sediment; acid; 1018; no sugar; albumin; amorphous urates; granular casts; leukocytes; epithelial cells.

The autopsy was performed by Dr. Ellis on the day of the boy's death. The pathologic diagnosis was chronic vegetative endocarditis of the mitral, aortic, pulmonary, and tricuspid valves; hypertrophy and dilatation of both ventricles; dilatation of the auricles; congestion of the lungs; adhesive pleuritis of the right side; chronic congestion of the spleen and kidneys; red atrophy of the liver, with serous cysts of the capsule, and beginning cirrhoses; chronic catarrhal gastritis; probably ulceration of the esophagus.

The heart was enormously enlarged. The right side and left

auricle were distended by partly clotted blood. The tricuspid valve showed over practically the entire margin numerous grayish elevations, most of them not over 1 mm. in diameter. The valve was not narrowed. The wall of the right ventricle was 0.9 cm. thick, firm, and red in color. The pulmonary valve had four cusps; the central point of each was thickened, and showed warty elevations. The left auricle was much dilated. The mitral valve was narrowed, the entire margin rough, calcareous, with extensions of the calcareous material to the bases of the leaflets and into the auricular wall for a short distance at two points. On the anterior auricular wall, 4 cm. from the valve, was a patch of calcareous deposit 5 cm. in extent. The wall of the left ventricle was 1.4 cm. thick, rather pale in color, but firm, the muscle columns being stretched. The endocardium, especially below the aorta, was gray and thickened at its margins. The edges of the aortic leaflets were everted, and showed bead-like rows of small fibrous elevations. Two of the leaflets were moderately adherent and contained calcareous deposits.

The liver was large, its capsule being much thickened. On the upper surface of the right lobe were several cysts, translucent, elevated above the surface one or more centimeters, most of them circular and 0.5 cm. in diameter. One was lobulated and 9 cm. in length. They contained a serous fluid, which was occasionally slightly gelatinous in content. The portion of the cyst wall next to the liver was formed by the thickened liver capsule, the cysts apparently being formed in the capsular adhesions.

The patient had a mitral obstruction of long standing, and more recent lesions of all the other valves. The clinical diagnosis was *double mitral disease as the chief lesion, with double aortic disease and tricuspid insufficiency*. The question of possible pulmonary insufficiency was considered, but the diagnosis was not thought to be justified in the presence of demonstrable aortic insufficiency, which, as is well known, is frequently characterized by a diastolic murmur as well or better heard along the left edge of the sternum from the second to the fourth rib than at the aortic area to the right of the sternum. The age of the patient, however and especially the presence of mitral obstruction as the dominant lesion and the persistence of cough, with marked pulmonary symptoms and cyanosis, deserved greater weight than they received as pointing to the probability of pulmonary insufficiency.

The special signs referred to by Gerhardt and Bamberger were not looked for, their papers not having come to the writer's notice at that time. It is doubtful if Gerhardt's auscultatory signs could have been elicited, for the right pleural sac was obliterated. In my second case they could not be heard, owing both to edema of the chest wall and to the presence of fluid in both pleural sacs.

CASE II.—The second patient was a white woman, aged thirty-six years, who entered the Philadelphia General Hospital November 10, 1912, complaining of cough, dyspnea, and epigastric pain upon coughing. She had first noticed swelling of the ankles seven weeks before admission. The first thing that attracted the patient's attention was pain in the knees; the feet then became so swollen she could not put on shoes for a period of two weeks, during which time she was compelled to go to bed. The swelling rapidly extended up the legs and thighs and the limbs involved became painful. After two weeks she got out of bed, but was compelled to return immediately.

Dyspnea was first noticed two weeks before admission to the hospital. It appeared during the night. The patient states that she was awakened by coughing, and felt as though she were going to choke. She was forced by her condition to leave bed and had to sleep sitting on a chair, with head inclined upon her arms and resting on a table. Up to the time of her admission she had been compelled to sleep in this manner. Cough has been continuous since it began.

The patient's father was living and well. Her mother died at the age of forty-one years. Acute indigestion and "dropsy" are said to have been the cause. Two brothers were living and well. Two sisters are dead, one at the age of eighteen months from "spasms," the other at the age of four years; the cause is said to have been a "heavy cold." One sister was living and well.

The patient does not remember having had the usual diseases of childhood. Had typhoid fever when eleven years of age. She uses alcohol in the form of beer moderately. Uses tea and coffee. Denies the use of drugs. She gives a history of having had a whitish discharge from the vagina which lasted three or four days, and cleared up under treatment by a physician. A burning sensation was noticed upon micturition.

The patient reached puberty at the age of fifteen years. Menstruation has been regular. She has had one child. The delivery was instrumental, and, as she states, resulted in a complete laceration of the perineum, which was repaired immediately after delivery. Child died at age of eighteen months. Cause is said to have been "convulsions and heavy cold."

The patient was a female adult, apparently thirty-five years of age. Skin was moist and cyanotic. Patient had anasarca, but was comparatively comfortable. Respirations were not hurried. Facial expression was one of anxiety.

The head showed no evidence of injury. The ears and nose were normal. There was no ptosis of the eyelids. The conjunctiva was pale. Pupils were equal and regular and reacted to light and distance. Convergence was good.

The lips were cyanotic. They showed no fissures and no herpes.

Buccal mucosa was pale; it showed no ulcerations nor mucous patches. Tongue projected in midline and was slightly coated. Teeth were in very bad state of preservation. Gums were spongy.

Chest: Expansion was poor but equal. Thorax was well developed. No scars, hemorrhagic spots, prominent veins nor abnormal pulsations. Apex beat was visible in fifth left interspace one inch to the left of the midclavicular line. A thrill was elicited upon palpation over the precordium. Fremitus was obtained posteriorly down to the angle of the scapulæ on both sides when in a sitting posture. Anteriorly it was obtained down to the fifth rib on the right side, while on the left it was obtained somewhat lower than this. While in the sitting posture fremitus was lost at least one and a half inches higher on each side than when the patient was lying down. The back of the thorax pitted on pressure. Percussion resonance was obtained down to the areas described above, then the note became dull anteriorly. Posteriorly below scapulæ it was flat. Harsh breath sounds were heard down to the fifth rib anteriorly on the right side. As the fifth rib was approached from the apex, rales were heard on the left side; rales were heard in the axilla as high as the third rib. Posteriorly, rales were heard all over the thorax above the angle of the scapulæ; below this rales were heard with distant breathing.

Heart borders: Second interspace, one inch to the right of the sternum and one inch to the left of the midclavicular line. There was a blowing systolic murmur heard best at the apex and transmitted to the axilla. A presystolic murmur not transmitted was heard a little to the right of the apex. Myocardial sounds poor.

The abdomen was distended. No organ or mass could be palpated through the edematous skin. Fluid was present within the abdomen as well as in its walls.

The extremities were markedly edematous.

Wassermann reaction positive.

The above notes made by the interne at the time of the patient's admission, represent fairly well her condition as it could then be discovered. In a few days, when I saw her, in addition to the usual physical signs of a double mitral lesion—presystolic thrill, short rough presystolic murmur with pronounced systolic sound followed by systolic murmur, accentuation of pulmonic second sound and some enlargement of the right ventricle—the patient exhibited a diastolic murmur best heard along the left edge of the sternum, with maximum intensity at the fourth left interspace. In a week after her admission a double aortic murmur could be heard. As it was not heard on her admission it was believed that an acute process had attacked the aortic leaflets. The pulse was of the Corrigan type, but the arterial signs could not be heard, owing to the edema of legs and arms. So, also, on account of edema of the chest wall and hydrothorax, Gerhard's chest signs could not

be elicited. The diagnosis was mitral obstruction and insufficiency, aortic insufficiency and obstruction, pulmonary insufficiency. The latter was not regarded as organic but as relative. The autopsy disclosed a lesion of the valve causing insufficiency.

AUTOPSY. By Dr. Ellis. Pathological Diagnosis: Hypertrophy and dilatation of both ventricles; dilatation of both auricles; buttonhole mitral; chronic aortic endocarditis, with superadded acute, vegetative endocarditis; chronic pulmonary endocarditis, with insufficiency; emphysema and edema of lungs; adhesive pleuritis on left side; congestion of spleen; chronic diffuse nephritis; red atrophy of liver; ascites; right hydrothorax; anasarca.

Body of an adult white female. Rigor mortis present. There was an intense subcutaneous edema. Peritoneum contained 300 c.c. of clear fluid. Intestines markedly distended. Left pleura showed universal adhesions. Right pleura contained 500 c.c. of serum. Heart was large; wall of the left ventricle was 1.8 cm. thick. Wall of the right ventricle was 0.7 cm. thick. Muscle was pale but fairly firm. Muscle columns flattened. All four cavities were enlarged. Mitral valve was a quite typical "buttonhole mitral," although margins were not excessively rigid. There was little or no calcareous infiltration. Aortic leaflets were thickened, rounded on margins, contracted, adherent, and rigid. Right leaflet showed in addition a more recent row of vegetations partly organized, nearly the length of "line of contact."

Pulmonary valves showed thickening fibrosis at the base of the left leaflet, with shortening of space between it and the posterior leaflet. Aorta showed moderate atheroma.

Lungs both showed moderate emphysema and extensive edema.

Spleen was large and firm; rich in blood; dark bluish red in color.

Kidneys showed moderately adherent capsules. Slight if any narrowing of cortex.

Stomach showed no gross changes.

Liver was a typical "nutmeg" organ.

Brain showed edema and edema of meninges. Skull thicker than normal.

I have quoted freely from Barié, Pitt, and Gerhardt because they have collected about four-fifths of the reported cases of a rare disease. One who has seen only a few cases must necessarily have an imperfect conception of it. The chief points in the diagnosis of pulmonary insufficiency are its frequent association with mitral obstruction, the diastolic murmur along the left edge of the sternum from the second interspace downward, the occurrence of marked pulmonary symptoms, with cyanosis, and the special phenomena pointed out by Gerhardt and Bamberger.

It is probable that relative pulmonary insufficiency occurs more

frequently then we are wont to believe. Cases have been reported by Graham Steel, Gibson, and more recently by Rudolph.⁶

It seems also to the writer not unlikely that in some of the cases of aortic insufficiency in which the diastolic murmur is heard best in the third and fourth interspace to the left of the sternum that the explanation may be an associated pulmonary insufficiency, usually of relative character.

THE TRAINING OF STUDENTS IN INTERNAL MEDICINE AT GERMAN UNIVERSITIES.

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I HAVE the more willingly availed myself of this opportunity to discuss the teaching of internal medicine in Germany, because I am in a particularly fortunate position to form an opinion on this subject, being able to observe the result of our methods not only from the standpoint of a university professor, but also from that of chief physician for many years to one of the largest hospitals in Germany. In the latter capacity, having maintained close relations with my professional colleagues in active practice, I have become acquainted with both the advantages and disadvantages under which they labor as the result of our modern method of instruction in internal medicine.

The German medical student does not begin his real clinical training until he has studied the preliminary branches during four to five semesters. These preliminary subjects comprise anatomy, physiology, physics, chemistry, zoölogy, and botany. The two last mentioned are regarded more as side studies, and are followed more for the purpose of teaching the student to think biologically than to train him systematically in these sciences. As a preparation for internal medicine, physiology, chemistry, and physics are of most importance.

The instruction in physiology is ample, since under the new requirements a candidate for examination must have had a laboratory course in this subject. On such solid scientific foundation the later pathological instruction can readily be built up. The instruction in chemistry in almost all the universities is in charge of the professor of chemistry of the college faculty, and therefore not in the hands of a medical man. This professor has under his direction the practical course in chemistry for the medical students. The fact that medical students are required to attend the same

lectures which are given to those studying chemistry as a profession has led to much discussion. Doubtless, instruction in chemistry restricted to subjects of particular importance to the physician would have this advantage: the subjects could be more thoroughly mastered because of their limited scope. This, however, is still a mooted question. For the present it seems advisable that the great questions of chemistry should be taught by a general chemist, rather than by one who is a specialist in only a small portion of this field. The same principle holds true for the instruction in physics. Moreover, at this period of the student's training the phases of chemistry and physics that are medically important are sufficiently emphasized in the courses in physiology. The question arises, however, whether it would not be an advantage to hand over officially to the physiological chemist and physicist at least the practical instruction of medical students in chemistry and physics.

During the fifth semester of this preliminary training, an examination, the so-called *Tentamen Physicum*, is held in these pre-clinical subjects, and not until this is satisfactorily passed can the "candidate in medicine," as the student is now called, be admitted to the clinical lectures; as a rule, therefore, the "candidate in medicine" enters the clinical lecture rooms with a good scientific foundation. This is, indeed, the case with gifted and industrious students. Unfortunately, however, a large portion of the student body on entering the university after the laborious and rigidly prescribed studies of the *Gymnasien* are inclined to enjoy too much academic freedom in the first semesters. Such men may perhaps acquire just sufficient knowledge to pass their examinations, but they do not take up chemistry and physics with the earnestness to be desired. As a result, their instructors in chemistry or physics fail to find in them a proper understanding of these subjects, and this lack of knowledge and interest is the more marked, because the majority of the students still come from "humanistic *Gymnasien*," that is, classical high schools, and begin their medical studies, therefore, with relatively less knowledge of the natural sciences, than do the smaller number of men coming from the more liberal atmosphere of the "*Gymnasien*" or "*Realschulen*." There has been a tendency of late to make the *Tentamen Physicum* so difficult that these deficiencies will be overcome at a time when the whole course of study can be easily changed, and the indolent student thereby prevented from continuing the study of medicine.

Before we take up in detail a description of the course of instruction in internal medicine, it would be well to call attention to the make-up of the teaching staff in the medical department of a German university.¹

¹ At some of the large universities, such as Berlin and Munich, it has become necessary to have a duplicate teaching staff.

The full professor is the *Ordinarius*. He is head of the department and holds the clinic. The next in rank is the chief of the outpatient department, or *Poliklinik*, and is usually called the *Extraordinarius*, or assistant professor. He is not a voting member of the faculty but is a regularly appointed teacher, and has in most cases his own institute. In addition there are a number of *Privatdozenten*, or associates; out of courtesy the older ones are sometimes referred to by the title professor. They hold assistantships in the clinic or *Poliklinik*. Some of the *Privatdozenten* who fail to advance and so become chiefs of the *Polikliniken*, and who, therefore, no longer retain their positions as assistants to the clinic, sometimes deliver certain minor lectures, but these should not be considered a part of the regular course of instruction. Now and then assistants who have not yet become *Privatdozenten* share in the giving of courses.

At this point I desire to call attention to the manner in which university teachers of internal medicine are developed. After the medical course is finished the graduate who intends to devote himself to an academic career begins as an assistant in the clinic, or *Poliklinik*. As competition for these posts is lively, the clinical teacher in charge often requires that before the young physicians receive clinical assistantships they shall fill similar positions in some of the pre-clinical branches. Thus it happens that they spend one or two years acquiring a special training in bacteriology, physiological chemistry, pharmacology, or pathological anatomy. The director of the clinic sees to it that he has among his assistants those who have had previous experience along the different lines of work just mentioned, with the idea that his assistants shall form a homogeneous whole, efficiently trained in all departments.

After an assistant has served, as a rule, three years as such, he becomes on presenting an acceptable scientific thesis a *Privatdozent*, and usually in three or four more years he may receive the title of Professor, provided he has proved his ability both as teacher and research worker. Obviously, it is only possible for a part of the assistants to be advanced to the real teaching positions of chief of the *Poliklinik*, or clinic. Inasmuch as the large municipal hospitals usually select the chief physicians of their internal medical divisions from among the university teachers, a strong stimulus is furnished to those in the subordinate teaching positions to at least win the title of Professor at the university. By this means their chances of becoming chief physicians to the hospitals are considerably increased. It is only recently that physicians who have completed their time as assistants in the hospitals have been considered for the chief positions. This has occurred, though rarely, in hospitals in which facilities are provided for carrying out scientific research studies. As a consequence of this slow development of the university teacher, a full professorship is, as a rule, not reached

until the thirty-fifth to fortieth year, and the position of chief of the *Poliklinik* seldom before the thirty-second year. This system also results in the assistants at the university clinics remaining as such for a considerable number of years, during which time no private practice is carried on. They therefore devote themselves entirely to ward work, scientific research, and to teaching. As the position of assistant is generally poorly paid, there must exist a real desire for scientific work in order to endure this long apprenticeship. For this reason we may point with just pride to our assistants, for such a thorough training in internal medicine as is acquired through being an assistant in a clinic for many years is almost unknown in other countries. Of course, a number of physicians in Germany after serving a shorter time as assistants enter practice. The majority of these become general practitioners, or after concluding their internship become assistants in various specialties. Those, however, who intend later to become university professors or chief physicians to hospitals must, as a rule, serve from seven to twelve years as assistants. It has always seemed to me that the chief advantage of this special training of the internist in Germany lies in this long period of assistantship.

We may now return to the description of the clinical instruction itself. During the first semesters after the preclinical years the student busies himself with the theoretical branches of pathology. He attends lectures on general pathology and on pathological anatomy. Heretofore this instruction was exclusively in the hands of the pathological anatomist, but of late, at a number of universities, the professor of medicine himself gives the lectures on pathological physiology, which must form the foundation of every truly scientific course in internal medicine. The majority of the students attend regularly these non-compulsory lectures, which afford a sure means of showing them that the science of medicine is a biological one, and of training them to think scientifically, thereby guarding them from the tendency later on of falling into mere perfunctory routine methods.

Aside from these theoretical lectures in the first clinical semesters the students attend courses dealing with clinical methods of investigation. These courses, which include methods of physical diagnosis, clinical chemistry, and microscopy, are frequently given by the younger members of the teaching staff, although many professors prefer to give themselves at least the theoretical part of physical diagnosis.

Instruction in the clinic now follows. As the professor of medicine is required to teach special pathology in as systematic and complete a manner as possible, he spends relatively a large amount of time in discussing separate cases. On the other hand the chief of the *Poliklinik*, who is responsible for the daily treatment of a large number of cases, is enabled to emphasize better the conditions

as they are met with in actual practice. This will be discussed in more detail later, because the arrangement of the course brings the student to the clinic before the *Poliklinik*.

Medical clinics in Germany differ according to the individual tastes of the professors in charge. Personally, and I believe the majority of my colleagues, prefer to discuss the individual patient before the clinic and not the disease alone. I lay great stress on teaching my classes to observe. On the other hand, many clinicians believe that the clinic is to be regarded as the place for lectures on special pathology and therapy with demonstration. It is obvious that this second method is only possible when a large amount of clinical material is available, and some are inclined to regard it, in spite of its being more systematic, as the poorer method. To be sure, every effort is made to bring together in the clinic as many cases of a given disease as possible, in order to illustrate the differences in the separate appearances of the disease. It is, however, a good plan to make all possible use of the clinical material at hand for purposes of instruction, even at the cost of systematic procedure, and I believe that this mode of instruction, varied in character as it at times must be, is more stimulating and advantageous to the student.

Fortunately, in Germany at all the universities, even those in small towns, there is a wealth of clinical material that suffices for all the needs of instruction.

At present, therapeutics is taken up in detail at nearly every clinic. The time is past for the treatment of disease to be regarded as of minor importance in clinical instruction.

In the clinic each student is called down on a case at least once to listen to what the professor has to say, and on not less than two occasions he takes actual part in the examination. On coming up for his state examinations the student must bring written proof that he has successfully performed his duties at the clinic. The functions of a *Practicant*,² as the student is called when he takes part in examining patients, are the following: As each case is brought before the clinic the clinical teacher calls upon the student and personally discusses the case with him. At the same time the student is questioned so as to bring out his knowledge of the subject. When this is deficient, he is assisted in his answers, rather than overcriticised before his fellows. By this means the instruction takes on a certain personal character. The *Practicant* must then keep the case under observation in the ward, and is charged with writing a record of the case, and, if the case be again brought into the clinic, is required to give information concerning its later

² This term is also used in another sense in referring to the young physician who, after completing his medical courses, is serving a prescribed practical year in a hospital (see later).—Translator's note.

course. I permit the *Practicanten*, in addition, once weekly to take part in making rounds in the wards.

In addition to the clinic, a number of special lectures are given. A really systematic lecture on special pathology today scarcely appears in any curriculum, as was formerly the case. Certain limited subjects, as, for example, nervous diseases, diseases of the digestive tract, or circulatory apparatus, are sometimes taught by younger members of the staff. On the other hand, therapeutics and diagnosis are always lectured upon in detail.

Within the province of internal medicine, electrodiagnosis and therapy, Röntgen diagnosis and therapy may be mentioned. Lectures are also given, as a rule, on dietetics, physical therapeutics, especially hydrotherapy, balneology, and balneotherapy. Lectures in pharmacology are given everywhere by a pharmacologist, who is in most cases a full professor, and has under his charge the theoretical and practical side of this branch. The practical application of therapeutics is also described in the clinic.

During the last semesters students attend the *Poliklinik*. The duties of the chief of the *Poliklinik* have been already referred to. His duty is to give those students who have already visited the clinic an insight into actual practice. This is accomplished first by the *Poliklinik* lecture, in which a large number of patients are shown and treated as they would be by a practising physician in his consultation hour. Emphasis is laid especially on the cases with slight ailments, which are not admitted to the hospital. Secondly, there is the *Distriktpoliklinik*. This provides medical attention for the poor as well as for certain citizens who by paying a fixed sum annually are entitled to avail themselves of it. This is the so-called *Kassenpraxis*. The city is divided into districts, and each student is assigned a district in which he must care for the sick. He reports his cases, and the chief of the *Poliklinik* or his assistants exercise a control over his work.

In Germany, during recent years, certain specialties have become separated from internal medicine. In this group pediatrics may first be mentioned. At most of the universities there are separate childrens' clinics, and at some smaller ones, where no pediatric clinic in a separate building is as yet available, there are at least childrens' and babies' wards, which furnish material for a special didactic clinic, entirely separate from the main medical clinic. The examination regulations call for written proof that the student has served as a *Practisant* in a childrens' clinic, this being a reason, if no others existed, for this separate arrangement. Although as professor of internal medicine I hold a clinic on pediatrics, I recognize the special position of this branch, especially as hygiene of the child in its earliest years and the diseases of this period must be dealt with in separate lectures.

In Germany nervous diseases are in part separated from internal

medicine, insofar as at some universities connected with the psychiatric clinics are wards also intended for nervous cases without mental disturbances. These clinics are officially named psychiatric clinics and clinics for nervous diseases. Nervous diseases will indeed continue to be taught in the medical clinics and such cases must be demonstrated. It is not a mistake that nervous cases, especially the functional neuroses, should be shown and demonstrated both by the internist and by the psychiatrist. The student then becomes acquainted with the nervous cases from two different but equally important standpoints, which can only be of advantage.

Furthermore, in Germany there is a growing demand for a separate course of instruction in so-called social medicine, which treats of practice connected with beneficiary societies, corporations, and life as well as accident insurance companies, the legal position of the physician to his practice, and the relations of physicians to each other. The majority of clinical teachers are opposed to making social medicine an independent subject for teaching. I agree with this view. The beneficiary societies and similar institutions are desirous of this step being taken, in the expectation that they will then receive better certificates from the physicians. This is an error. Only he who has learned to make a proper medical examination can write a useful certificate of health. It is the duty of the clinical teacher to point out the importance of and the formalities concerning a certificate of health, as well as to enlighten the students on the highly developed system of beneficiary and insurance bodies which exist in Germany. This he is competent to do, as he has practical experience in such matters.

After following this short description of the instruction in internal medicine at our universities, if one asks, Does it fulfil its purpose? this question unfortunately can only be answered conditionally in the affirmative. Without doubt the course of instruction is of such a character that an industrious student receives a sufficient scientific training. Experience he must acquire later. For this the time, five years, devoted to medical study is too short. There is, however, another reason why the training in internal medicine is rendered difficult. Our students are overworked in their five clinical semesters. They study not only internal medicine, but are also expected to acquire a knowledge of surgery, gynecology, and obstetrics. Not only these but also special subjects are continually being introduced into the regular course of study. Hygiene requires a great deal of time. Diseases of the eye, ear, nose, and throat, as well as psychiatrics, are already subjects upon which the student is examined or is soon likely to be. The same holds true for dermatology, orthopedics, and other subjects. Our students in the clinical semesters are fairly industrious throughout. They attend in Marburg eight to ten lectures daily. This, in my opinion,

is more than the working capacity of a normal brain can endure. The student is scarcely able to do any work at home, and for this reason our university vacations are an absolute necessity, in order to give the student time to study.

The danger is that in the near future the study of internal medicine will be too much limited through the encroachments on both the time and working capacity of the students by the special subjects. For example, it is only possible for comparatively few students to serve in the *Distriktpoliklinik* during the semester. To a certain extent this is offset by the fact that in the last semester many students remain at the university during the vacations, work in the clinic, or *Poliklinik*, and indeed, as so-called under assistants, take part in active hospital service. This is also possible during the semester, but the number of such positions is of course limited.

The administrative authorities have become convinced that the student cannot acquire from his university instruction alone sufficient experience and self-dependence. On this account the so-called practical year has been introduced. This means that every student must serve at an officially recognized institution for the sick after the state examinations have been passed. Not until this practical year has been finished is a license to practice granted. Four months of this year must be given to the medical wards, the remaining time being left free for other branches. The right to accept these *Practicanten* belongs to almost all hospitals, and in part to the sanatoria for tuberculosis and to the insane asylums. The academies for practical medicine in Cologne and in Düsseldorf are considered to have as their special duty the training of *Practicanten*. Unfortunately, the present lack of assistants in Germany, the causes of which I will mention later, has led smaller hospitals, which could not fill their assistantships, to engage *Practicanten* in place of assistants, and, indeed, to give them free lodging and perhaps a salary as well. As a result, these positions are more sought after than those in the great hospitals, which offer no return for services, but much more opportunity to learn. Moreover, as a rule, in these last institutions the staff is composed of physicians better adapted to be teachers.

Recently the attempt was made to do away with this unfavorable state of affairs through suitable regulations. It was suggested that the *Practicant* be put in charge during his practical year of a ward consisting of at least fifteen beds; the assistants or the chief physicians to exercise, however, control over these patients. There is no doubt that the practical year is a valuable institution, although in Germany many contrary opinions in regard to it have been heard.

The practical year has been the cause of at least one unfortunate condition. Young doctors of medicine in the past, after passing their state examinations, usually became the representatives of

physicians who wished, for various reasons, to give up their practices temporarily. It is now difficult for such physicians to find qualified individuals to take over their work. For this fact the practical year is in part responsible. Another reason, however, is that many young physicians after ending their year of practical duty in the hospitals become assistants, and after completing their time of service as such go into practice without being inclined to temporarily care for the practice of another.

We now come to a consideration of the subject of assistantships other than those in the university clinics which have already been described, that is, the positions of assistant to the city and other hospitals. Before the introduction of the practical year it was the custom for young physicians who could in any way afford financially to do so, and were not forced to turn at once to earning a living, to enter upon assistantships of some years' duration in various hospitals. This was done by those who did not find positions in the university clinics. They would, as a rule, spend approximately one year in medical wards and one or more years in the surgical or other divisions. These men who obviously were more experienced than their colleagues, who went directly from the university into practice, later on acquired a practice more rapidly. At present these conditions have become essentially changed. While formerly there was sharp competition for the comparatively few available assistantships, and often the young physicians had to content themselves with unpaid voluntary positions, there is today in Germany a considerable lack of assistants, owing to the rapid development of the hospital system. It should here be noted that hospital assistants carry on no private practice in addition to their hospital service. In almost every town hospitals have been founded, and in the larger cities there are some hospitals with a great number of beds. The beneficiary societies of miners and those in other callings, the life and health insurance corporations, have, in addition, large hospitals and sanatoria for tuberculosis, without mentioning the numerous hospitals founded by religious orders, which are to be met with in the Rhine districts and in Westphalia. All these institutions require medical assistants. Here, too, may be mentioned private institutions which support physicians of reputation. This lack of assistant material has been the cause of the hospital positions being, if not well paid, still better paid than formerly, so that in contra-distinction to the as yet low-salaried university assistantships the young assistant physician in a hospital may be said to receive sufficient income to support him so long as he remains unmarried. While formerly the smaller hospitals supported surgeons as physicians in chief and were preponderately surgical in equipment, there are now being instituted independent divisions for internal medicine.

As a result of these conditions only a small number of the young

medical men go directly into practice. The large majority become assistants, and so complete their training. The positions of chief physician are held for life and are comparatively few in number. The number of assistants naturally far surpasses the number of chiefs. In most cases the assistant period is not to be regarded as a training for the position of chief physician, but is rather to be looked upon as a preparation for active practice, especially as the more important positions of chief physician are usually filled from the ranks of the university teachers.

The young doctor of medicine, after serving on an average of two to three years as an assistant, on entering into practice does not always find there the most pleasant conditions. The medical profession is today overcrowded in Germany. Hence, the average income of the physician is comparatively small and totally inadequate as compared to the length of the training required. For this reason, many practitioners are later forced to become connected with corporations, beneficiary societies, and similar organizations and so earn a certain *pro rata* remuneration, which even if fair, is not, in view of the great numbers of cases that must be seen, conducive to scientific development. If the *Kassenarzt*, as such a physician is named, be placed in the position, as occurs in the industrial districts, of having to treat thirty to forty patients in his office hour, he must sacrifice care and thoroughness of examination in order to accomplish it.

It is recognized that the practice of internal medicine of today, scientifically pursued, demands a number of laboratory examinations for which the busy practitioner has neither the facilities nor the time at his disposal. Such examinations can scarcely be properly paid for by the people at large. The attempt of late is being made, at least in the cities, to relieve this unsatisfactory condition by instituting laboratories for this purpose and by having the physicians refer their complicated cases to the hospitals for diagnosis. As the practitioners, earlier in their careers, were usually assistants to the hospitals, they often maintain in this way gratifying connections with hospitals and with scientific medicine. In the country it is difficult to carry out this plan, and I believe this is precisely the reason why physicians of a better class do not willingly take up country practice. Of course, there are many excellent physicians to be found in rural districts who continue to work scientifically; and, because they must be self-reliant, frequently surpass their city colleagues in general medical knowledge.

It is natural that the busy practitioner cannot always follow the rapid progress, which the science of medicine and internal medicine especially is making. A splendid proof of scientific interest is shown by our German physicians who support so well the post-graduate courses, which are held at the universities, academies of medicine, and in the larger hospitals. These courses, which,

as a rule, last some weeks, can only be taken by the practising physician at a considerable cost, which includes loss of practice and paying another for taking over his work, in addition to the sacrifice of time that might otherwise be devoted to vacation. In Cologne, I held such graduate courses for a period of six years, and it was almost always the course in internal medicine which could boast of the best attendance. The average German practitioner possesses a live interest for scientific medicine.

It would seem, therefore, that the training of physicians in the medical science, and especially in internal medicine in Germany, is sufficient to meet all reasonable requirements. There are, of course, physicians of inferior standing in this country who by an effort have been able to pass their examinations and who do not develop later, but fortunately these form a small minority, and rarely advance to good medical positions. The German who today dedicates himself to the study of medicine must have clearly in his mind that he is to lead a life filled with labor; but if he possess ability, a life replete with the labor that breeds contentment, even though it fails to bring with it a large income.

A STUDY OF THE NORMAL COAGULATION OF THE BLOOD, WITH A DESCRIPTION OF THE INSTRUMENT USED.

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THIS brief study is more of a test for the stability and accuracy of this new instrument than a study of the coagulation time of the blood. We have tried so far as possible to eliminate the intrinsic factors which might affect the blood by choosing normal adult individuals. The intrinsic factors are as follows:

1. Those affecting the blood: (a) Viscosity; (b) blood pressure; (c) leukocytes; (d) specific gravity and anemia.
2. Physiologic conditions of the body: (a) Age and sex; (b) menstruation period; (c) time of day; (d) diet.

In the testing of any new instrument for the estimation of the coagulation time the extrinsic factors are the important ones to overcome.

The extrinsic factors are as follows: (a) Foreign body—dust or dirt; (b) area of surface contact; (c) air evaporation; (d) temperature; (e) size and shape of drop; (f) mechanical disturbances; (g) determination of end point.

We have taken the best parts of the numerous instruments on the market and combined them, thereby obtaining what we think is a simple but reliable instrument. In over three hundred tests we have found the average time to be from three and one-half to five and one-half minutes.

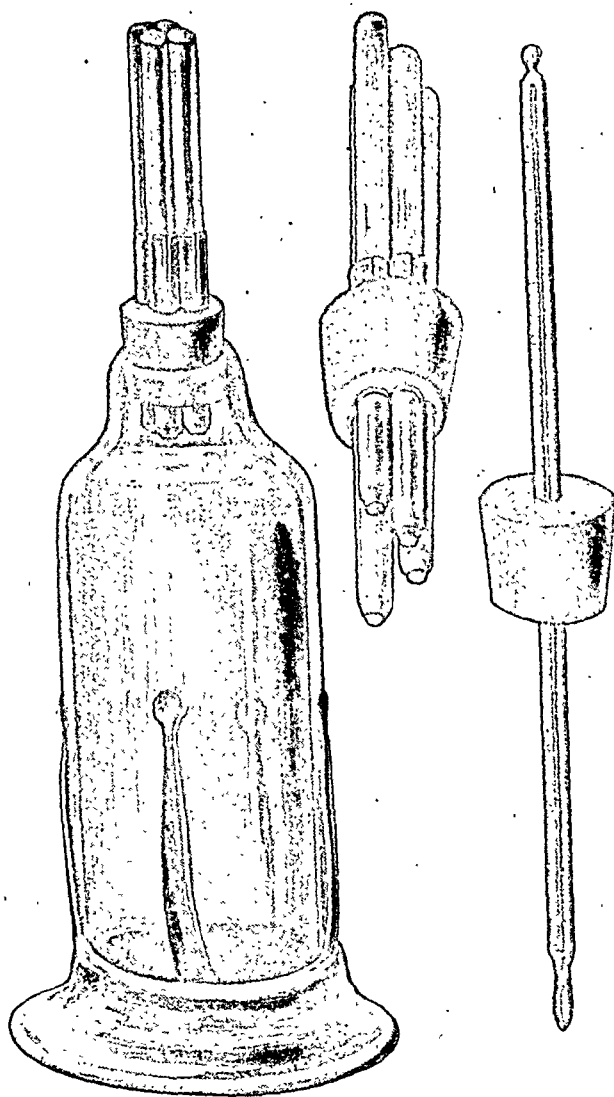


FIG. 1.—Showing various parts of the instrument.

DESCRIPTION OF THE INSTRUMENT (Fig. 1). It consists of an eight-ounce thermos bottle without the silver lining, an aluminum stand, and two rubber corks which fit snugly into the bottle. One cork has a hole in it for a thermometer which registers up to 140° F. The other cork has four openings, each of which is lined with a brass flange. Into each of these openings a glass rod fits. These rods are four and one-half inches long with a diameter of 8 mm. One end is cone-shaped, with a flat tip 4 mm. in diameter. The

other end is slightly bulbous, to prevent the rod from slipping through the flange.

METHOD OF APPLICATION. The thermos bottle is filled with water at 98° F. to within one inch of the top. It is then covered with the cork containing the thermometer to prevent any change in the temperature of the water. The rods within the second cork are first scrubbed with soap and water and then cleansed with alcohol and finally with ether. This cork is then substituted for the one containing the thermometer, so that the rods will become heated to the temperature of the water. This is done while the finger of the patient is being prepared. The rods during the time that they are in the bottle heating up to the temperature of the water will have collected considerable moisture, and it is therefore necessary to wipe them dry before collecting the blood, else the moisture will dilute the drop of blood. The finger is given a good stick, so that it bleeds without pressure. The first drop of blood is wiped off, and as soon as the second drop or whatever drop you are going to use appears. As soon as the drop begins to appear the cork containing the glass rods is removed from the bottle and the rods are wiped dry. Then with care each one of the rods is placed in contact with the drop of blood. If done carefully the same size drop will be taken up by each rod. From the time of the appearance of the drop until the blood is collected and the cork replaced in the bottle should not be more than ten seconds.

The end point with this instrument is determined in three ways:

I. In explaining the end results we shall number the glass rods in the order in which the blood was collected upon them. At the end of two and one-half minutes rod No. 1 should be pushed down into the water. It will be noted that all the blood falls off the end of the glass rod and breaks up into a fine cloud. Rod No. 2 is introduced into the water at the end of three and one-half minutes. There will still be considerable falling off of the blood, but when it breaks up the particles will be coarser and there will remain a small amount on the end of the rod. Rod No. 3 is introduced into the water at the end of four minutes. There will still be noted some dropping off of the blood, and there will be found a larger amount of blood adherent to the end of the rod. Rod No. 4 is introduced into the water at the end of four and one-half or five minutes, depending upon the action of the former rods. There will be a slight falling off, but the greater part will be found to be adherent to the end of the rod if coagulation has taken place. The fact that we start at two and one-half minutes from the time of the appearance of the drop is only an arbitrary factor. The test can begin at any time and the rods be introduced at any time that the operator desires.

II. The cork containing the four rods is now removed from the

bottle and held up to the light, with the end on which the blood is adherent nearest to the eye. On looking through the rods the following results will be found: Rod No. 1 will be clear. On Rod No. 2 will be observed a slight reddish tinge. On Rod No. 3 this reddish tinge will be somewhat deeper in color and the end of Rod No. 4 will be almost covered with a red clot.

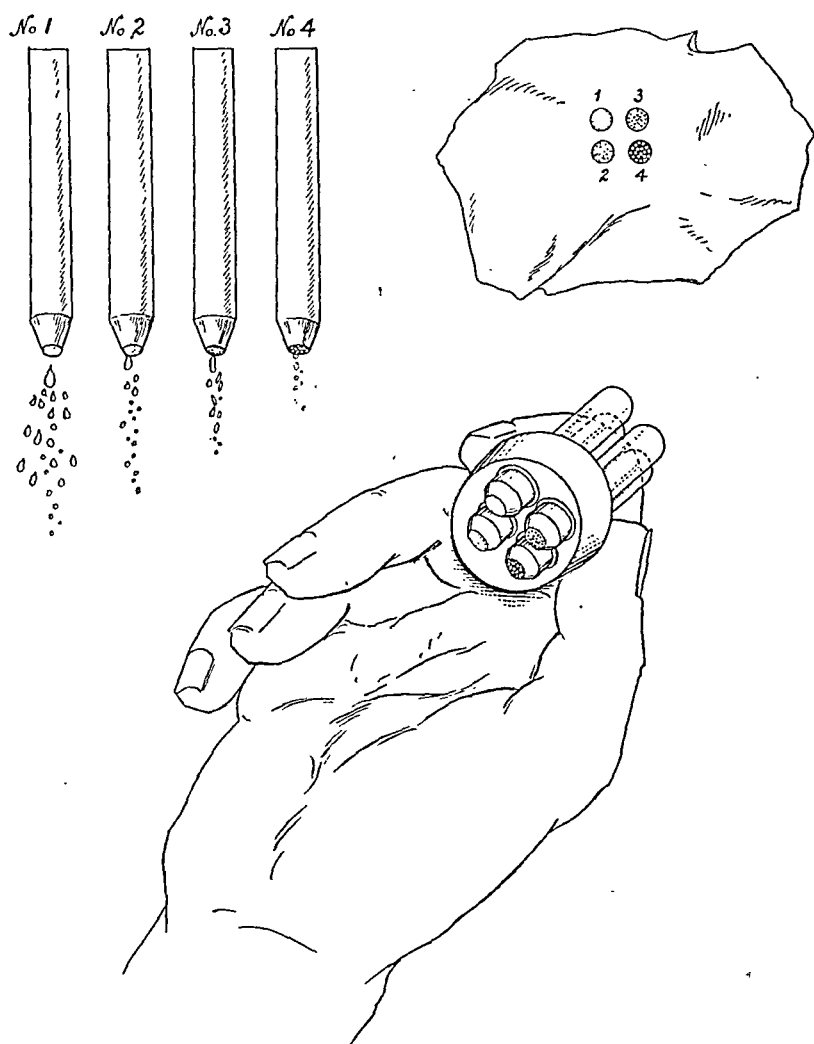


FIG. 2.—Method of application.

III. The end of each rod is blotted with filter paper or blotting paper, as shown in Fig. 2. The blot made by Rod No. 1 will be practically clear. Rod No. 2 will show a slight red color, Rod No. 3 will show a more distinct red, and Rod No. 4 will show a clot. If the last rod does not show the blood to have coagulated the test should be repeated, with the first rod introduced at four minutes and the others at either one-half minute or one-minute interval.

It is a well-established fact that the first drop does not coagulate as rapidly as the later ones, and as we want to know the shortest time we take about the fourth or fifth drop. Blood that is taken from the veins and does not come in contact with the tissue juices does not give the true clinical coagulation time. The tissue juices are one of the most important factors in the causation of coagulation.

An almost complete bibliography and description of the different instruments used for determining the coagulation time can be found in Dr. Myer Solis Cohen's article, "The Coagulation Time of Blood as Affected by Various Conditions."

I am indebted to Dr. Allen J. Smith and to Dr. Ludholts for suggestions and criticisms.

Messrs. Chas. Lentz & Co., Philadelphia, have placed the instrument on the market.

CHRONIC ULCER OF THE PYLORUS (DUODENAL AND GASTRIC) SECONDARY TO APPENDICITIS, COLITIS, BILE-TRACT INFECTION, AND OTHER FOCI OF INFECTION WITHIN THE AREA DRAINED BY THE PORTAL VEIN.¹

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THE history of the modern study of "stomach trouble" may easily be arranged into three periods. It has not been many years since we heard much and long of the stomach specialists. These gentlemen on the medical side were treating the organ with bitter and acrid medicines, dietetic restrictions, the stomach tube, electricity, and other remedies; and certain enthusiastic surgeons were coupling the stomach to the bowel under the mistaken impression that they were diverting an imaginary, harmful digestive fluid from an imaginary sore spot in the region of the pylorus. In reality the "stomach specialist" was often treating an organ guilty only of making known the symptoms referred to it from such lesions as chronic appendicitis, bile-tract infection, pancreatitis, pulmonary, cardiorenal, brain, spinal cord, and other diseases, or presenting only slight pathology, and that of secondary development.

In the second period it was asserted by many that nearly all "stomach troubles" were in reality not stomach diseases at all, but only "reflex symptoms" indicating disease elsewhere. During

¹ Read at the meeting of the Medical Society of Virginia, held at Norfolk, Virginia, October 23, 1912.

this period physicians used pills, sedatives, electricity, and olive oil, and surgeons were uncoupling gastro-enterostomies "done elsewhere" and removing appendices, gallstones, and other "reflex" causes; believing that because certain individuals could swallow nails, lamp-chimneys, knife-blades and other such articles and still have good digestion, that the stomach was almost immune to disease. During this period the stomach was designated by a short and very ugly word; little or no attention being paid to the secondarily produced pathology in the stomach resulting from long-continued disease in correlated organs.

About the year 1910, however, largely through the work of clinical pathologists, and especially of MacCarty, the true condition of affairs became suspected, and the pendulum of judgment began to take its proper position. So that while it is granted that the stomach is often making known the symptoms referred to it from disease in remote areas, yet it becomes the seat of real pathology as a late result, especially of appendicitis, bile-tract disease, and other lesions in the area drained by the portal vein. It is known that in the patient who has persistently impaired gastric function, as shown by delay of digestion, impaired motility, dilatation, and especially diminished hydrochloric acid, with excessive mucus in the gastric contents, the stomach upon examination will show thickening of the mucous membrane, with submucous infiltration and hyperplasia, and this means chronic inflammation.

During the last few years much information has been gained, and if we will acquire, assimilate, and appropriate the knowledge now accessible, most of the problems connected with pyloric ulcer will be advanced toward solution. The significance of clinical experience, corroborated by scientific facts given us by anatomists, physiologists, and a study of living pathology, would cause most of the strange hypotheses, curious fancies, and absurd statements so carefully embalmed and persistently transmitted from one text-book to another, soon to give place to a proper conception of the real cause not only of ulcer, but of a train of allied disorders which for centuries have masqueraded as and finally produced real stomach disease.

The earliest cases of pyloric ulcer discovered upon the operating table were those in which perforation had occurred, producing diffuse peritonitis, and in which the pre-operative diagnosis of acute fulminating appendicitis had been made. A detailed study of the case reports of perforated duodenal and gastric ulcer, operated upon even as recently as three to five years, shows that there was a frequency in this particular error of diagnosis. Gibbon and Stewart,² for example, report 22 cases of perforated ulcer operated upon, in 6 (27 per cent.) of which the diagnosis of appendicitis

² Transactions of Surgical Section, Amer. Med. Assoc., 1909.

was made before the operation, a "chronically inflamed" appendix removed, and further search revealed perforated duodenal ulcer. The remaining 16 cases were diagnosticated as perforation of the duodenum, and the appendix was not examined. Ellsworth Elliott's cases³ showed the same tendency to disregard the appendix except when a diagnosis of appendicitis was made. In the olden days even the surgeon's consideration of appendicitis was an acute suppurating organ, with or without peritonitis, and what is now known as chronic appendicitis—namely, obliterated, thickened, kinked, adherent appendices—were often regarded as insignificant. During this time many cases of bile-tract infection, with and without stones, were discovered during the course of operation and at autopsy.

For the past two or three years, however, the journal articles have described, with progressive frequency and lucidity, without, in many cases direct intention of calling attention to etiology, a large number of cases in which associated lesions were found in the pylorus, bile tract, appendix, pancreas, and the area drained by the portal vein. And while associated lesions in this physiologic area are frequent there is a scarcity of incidental lesions elsewhere in the body when studied in comparison. Previous to 1910 figures were comparatively scarce. It is only during recent years that exploration of the abdominal contents to discover lesions other than those for which the incision was made has been carried out; and yet there are mentioned in some contributions instances of association of these lesions found sometimes at the primary operation or more frequently at a second operation or at autopsy.

Thus the Mt. Sinai Hospital report for 1904 shows 7 cases of ulcer operated upon; 3 of these were associated with foci of infection within the area drained by the portal vein, 1 with appendicitis, 1 with bile-tract infection, 1 with "spastic ileus." In January, 1906, Ochsner⁴ recorded 4 cases of pyloric ulcer, 2 associated with bile-tract infection, 2 with appendicitis, and 1 case with all three lesions. In February, 1907, Moynihan⁵ recorded 15 perforated ulcers; 1 case had incidentally an inflamed prolapsed rectum. In the other cases the appendix and bile tract were not examined. (In patients with pre-operative diagnosis of perforation, exploration is not commonly carried out; the surgeon is too busy saving life, to look for other troubles.) In 1908 Moynihan⁶ recorded 205 cases of ulcer, 10 of which (5 per cent.) required bile-tract drainage. Again the appendix was not examined. In 1908 Deaver⁷ reported 66 cases of ulcer and its results, in 15 of which (nearly 25 per cent.) the history of dysentery, typhoid fever, appendicitis, and bile-tract disease were elicited or demonstrated. In 1909 Gibbon and

³ Amer. Jour. Surg., October, 1908; January, 1909.

⁴ Annals of Surgery, January, 1906.

⁵ Ibid., June, 1908.

⁶ Ibid., 1907.

⁷ Ibid.

Stewart⁸ reported 22 perforated ulcers, 6 of which were diagnosed before operation as appendicitis and a chronically diseased appendix removed.

In 1910 MacCarty and McGrath⁹ from pathologic material derived from operation and autopsy studied the relation of appendicitis to bile-tract disease and gastric and duodenal ulcers. Of 52 cases of ulcer, 26.9 per cent. were associated with chronic appendicitis. Of 175 cases of bile-tract infection, nearly 50 per cent. of the cases were associated with chronic appendicitis. Of 2000 cases of chronic appendicitis operated upon, 8.7 per cent. were found to have in addition, bile tract infection. Three cases of duodenal ulcer were discovered at autopsy after operations for bile-tract infection. These gentlemen "regard the evidence sufficient not to prove, but to stimulate a careful study of the clinical histories, with relation to the possibility that chronic inflammation in the appendix reflexly disturbs the gastro-duodeno-hepatico-pancreatic physiologic system, thereby bringing about conditions whereby such lesions as gastric ulcer, carcinoma, duodenal ulcer, bile-tract infection, and pancreatitis may be indirectly produced."

Deaver recorded, in 1910, from the German Hospital clinic, 4 cases of ulcer, 2 with bile-tract infection. Frazier,¹⁰ in the Episcopal Hospital, 1910, operated upon 5 ulcers, 1 with appendicitis and 1 with bile-tract infection. Ochsner¹¹ and many others are on record as having operated upon many single cases in which appendicitis, bile-tract infection, and ulcer were all found in the same patient at the same time. Beckman¹² records from the Mayo clinic in July, 1910, 20 cases of ulcer operated upon, and in 3 of these bile-tract drainage was also required. Fenwick, quoted by Wood,¹³ in 1910, records 61 cases of ulcer, 9 of which revealed also chronic appendicitis. In Augustana Hospital reports, 1910 and 1911, are recorded 79 cases of ulcer operated upon; 35 (or 44.3 per cent.) of these had also chronic appendicitis; 14 (or 17.7 per cent.) had also bile-tract infection, with or without stones, demanding drainage; 7 (or 8.8 per cent.) had all three lesions together, and required appendectomy, bile-tract drainage, and gastro-enterostomy; 3 cases (or 3.8 per cent.) had also to be operated upon for hemorrhoids, and prolapse of the rectum. Mitchell¹⁴ reports 48 cases of pyloric ulcer operated upon in fourteen months, and 19 of these (or 39.5 per cent.) were associated with chronic appendicitis. MacCarty and McGrath's 52 cases¹⁵ showed 26.9 per cent. associated with chronic appendicitis. Moynihan,¹⁶ in 1910-11, operated upon

⁸ Transaction of Surgical Section, Amer. Med. Assoc., 1909.

⁹ Annals of Surgery, May, 1910.

¹⁰ Internat. Clinics, July, 1910.

¹¹ Surg., Gyn., and Obstet., September, 1910.

¹² Annals of Surg., December, 1911.

¹³ Monograph, Duodenal Ulcer, 1912, 2d edition.

¹⁴ Ibid., October, 1911.

¹⁵ Ibid.

¹⁶ Ibid., May, 1910.

62 cases of ulcer, 6 of which demanded also bile-tract drainage, for infection with or without stones, 25 cases had also chronic appendicitis, 2 cases had appendicitis, bile-tract infection, and ulcer all operated upon at the same time, and one case had also tuberculosis of the bowel. From May, 1910, to December, 1911, 34 cases of ulcer were operated upon by Moynihan, and in 21 also appendectomy was performed for chronic appendicitis. This observer¹⁷ studied 14 consecutive cases of pyloric ulcer, with the view of determining the condition of the appendix, and having an artist make a sketch of the condition of the appendix in each case. In 2 of these cases the patients were so ill that the appendix could not be removed; in all the remaining 12 the appendix was the seat of chronic disease, sufficiently severe to demand its removal independently of gastric ulcer. Moynihan has no hesitancy in stating that he believes that the appendix should be removed in at least 90 per cent. of all cases, and that in 80 per cent. of these it is the seat of long-standing and advanced disease.

Of a total of 332 cases of ulcer operated upon in 1910-11, in 111 (or 33.3 per cent.) there was also chronic appendicitis sufficiently severe as to demand appendectomy; and this proportion, be it remembered, is far below the actual facts, for in comparatively few was the appendix even examined. Pilcher,¹⁸ in 100 cases of histologically proved chronic gastritis, with occult hemorrhage, found 48 with appendicitis; 36 with appendicitis only, and 12 with appendicitis and bile-tract infection combined. Sixty cases had in addition to stomach infection, bile-tract infection, and of these, 32 had gastric and bile-tract infection together, 16 had gastric, bile-tract, and pancreatic infection combined, and 12 had gastric infection, bile-tract infection, and chronic appendicitis. In only 16 was gastric infection alone present.

Considering cases operated upon for bile-tract infection with and without stones the following incidence of ulcer, bile-tract infection, and appendicitis is interesting: In January, 1906, Ochsner¹⁹ reported 13 cases of bile-tract infection, with and without stone; and 4 of these had in addition pyloric ulcer, 7 had appendicitis, 1 case had appendicitis, pyloric ulcer, and bile-tract disease all combined. Of 344 cases of bile-tract disease studied by Stanton²⁰ in 1911, which had been operated upon eight or nine years previously, it was noted that 9 of these cases had ulcer of the stomach also. In the Augustana Hospital, 1910-11,²¹ 141 cases of bile-tract infection were operated upon, 5 of these had in addition ulcer, of these 2 had appendicitis, ulcer, and bile-tract disease combined. Sixty-eight cases (or 48.2 per cent.) showed also chronic appendicitis, 1 case had

¹⁷ Moynihan, *Lancet*, January 6, 1912.

¹⁸ *Jour. Amer. Med. Assoc.*, November 19, 1910.

¹⁹ *Annals of Surgery*, January, 1906.

²⁰ *Jour. Amer. Med. Assoc.*, August 5, 1911.

²¹ Augustana Hospital Report, 1910 to 1911.

pancreatitis, and 2 cases had hemorrhoids. According to this incidence, 3.5 per cent. of all cases of bile-tract infection are complicated by ulcer of the stomach.

Considering chronic appendicitis, the Augustana Hospital, 1910-11, reports 514 cases, 7 (or 1.3 per cent.) of which had ulcer of the stomach, 2 of these had ulcer alone and 5 had ulcer and bile-tract infection; 45 cases (or nearly 9 per cent.) had bile-tract infection without ulcer. Fenwick, quoted by Wood,²² found that in 31 cases of appendicitis, 9 of them, nearly 29 per cent., had pyloric ulcer and of 61 cases of ulcer, 9 (or 14.7 per cent.) were associated with chronic appendicitis, and 3 cases (5 per cent.) with bile-tract infection. There are many single and small groups of cases in literature easily accessible, but the clinical reports of most cases are incomplete. The writer would suggest that the coincidence and relationship of these lesions, one to the other, be more carefully investigated, and that table findings be more fully recorded. Doubtless active surgeons are doing this the world over at the present time, and it is to be hoped that further studies will be rapidly forthcoming. I have observed in my own practice and through the courtesy of several local surgeons during the past year at least a dozen cases in which chronic appendicitis, bile-tract infection, and pyloric ulcer existed in the same patient at the same time. And in conversation with several of my friends I have heard of many more cases. This subject is too large and important to be based only upon "experience," and I shall therefore avoid contamination of facts with deductions founded upon "personal observation." After all, clinical experience, to be of value, must be based upon a large amount of scientifically studied material and unless the clinical deductions can be shown to be in conformity with established facts of physiology, pathology, and anatomy, the experience cannot be productive of positive conclusions.

The association of pyloric ulcer with acute appendicitis and other acute infections of the portal area presents a striking rarity of incidence. Clarence McWilliams²³ reported from the Presbyterian Hospital, New York, 687 cases of acute appendicitis. Of these 68 died and only one showed evidence of ulcer in any part of the bowel. In none of those cases which recovered was there any sign of pyloric ulcer. McWilliams quotes from Schwalbach, who collected 30 cases of gastric and intestinal hemorrhage after operation for appendicitis, and this observer believes that the hemorrhages in these cases were caused by septic thrombi of the omentum and mesentery. Many cases of portal phlebitis complicating acute appendicitis are recorded in literature, but this is indicative only that infection is carried from the appendix by way

²² Surg., Gyn., and Obst., September, 1910.

²³ Annals of Surgery, June, 1910.

of the portal vein. Abscess of the liver, subdiaphragmatic inflammation, and acute bile-tract infection (cholecystitis and cholangitis) are common enough as later developments during the course of acute appendicitis. Duodenitis and gastritis are present in all cases, except those operated upon very early; but chronic ulcer is not to be expected as a result of acute, promptly cured, appendicitis.

As to the coincidence of chronic appendicitis with other lesions within the abdomen, many practitioners believe chronic appendicitis to be such a frequent finding that the thickened, obliterated, or flimsily adherent appendix will be noted with equal frequency if sought for during the course of operations upon other intraperitoneal structures. But the figures and observations of pathologists fail to show anything like the same frequency as is noted in cases of bile-tract disease and pyloric ulcer. Only 17 per cent. of all autopsies and 23.5 per cent. of all abdominal operations including those for lesions of the bile tract, pyloric, etc., show any evidence of disease of the appendix (MacCarty). With right-sided salpingitis we are familiar with the associated appendicitis incident to extension of infection along the appendiculo-ovarian ligament of Clado. In no other pelvic disease, however, is the incidence of appendicitis noted with anything like the frequency as is the case with bile-tract and pyloric infections. Nor is ulcer found with any significant frequency. Thus in Augustana Hospital, 1911, of 69 cases of uterine myomata, ulcer was not found in a single case; and appendicitis was found only 19 times. In only 1 of the ulcer cases in the Augustana Hospital was there recorded an apparent lesion in the pelvic organs and this was a case of retrodisplacement of the uterus and chronic appendicitis. Of 1244 myomas operated upon by Mayo,²⁴ in only 1 was pyloric ulcer recorded, only 92 had gallstones, and in only 686 was the appendix removed. Of 100 women operated upon for gallstones in the gynecologic clinic of John G. Clark,²⁵ about 70 sought relief for female pelvic disease and 14 for other abdominal lesions, producing symptoms more acutely crippling than those caused by the bile-tract disease.

Sixty-four years ago Curling claimed to have noted the occurrence of ulcer in the duodenum secondary to burns, but there have been surprisingly few of such cases reported in literature. Ulcer following burns is always of acute type, occurs within seven to fourteen days following the burn, and never on the gastric side of the pyloric ring (Murphy).²⁶ The causative agent in such cases is believed to be irritative toxic material eliminated by the bile. When the abdominal wall is burned, septic material may pass through the vein, passing in the round ligament from the umbilicus to

²⁴ Surg., Gyn., and Obst., February, 1911.

²⁵ Jour. Amer. Med. Assoc., November 2, 1912.

²⁶ Gynecology and Abdominal Surgery, Kelly and Noble

the portal vein and through the liver into the bile and the duodenum. In the cases reported by Roberts²⁷ of duodenal ulcer coincident with wounds of the urinary bladder, or kidneys, general septic processes and burns, the evidence that chronic ulcer of the duodenum was caused by or even consecutive to wounds and infections of the urinary organs is lacking and the cases too few to attract serious attention even to the incidence. In the case of his own the ulcer was of the chronic type, with indurated margins, and was found at autopsy twenty-six days after a rupture of the bladder, with fracture of the pelvis. No mention is made of the absence of infection in the bile tract or in the area drained by the portal vein. Chronic duodenal ulcer can hardly form in so short a time as twenty-six days. Melchoir²⁸ reported from literature 9 cases of ulcer found at autopsy in patients who had had amputation performed. He further states that in general autopsy findings 0.4 per cent. show ulcer of the pyloric region, whereas in the autopsy findings in cases of death following septic processes in 2.7 per cent. ulcers are found, and following extensive burns 3.3 per cent. of cases at autopsy show duodenal ulcer. These cases are of acute ulcers, and according to the testimony of most observers, acute ulcers do not become chronic.

Apart from the operating-table evidence of the association of chronic appendicitis and bile-tract infection with pyloric ulcer, there are striking clinical features possessed in common by these separate diseases. They all exhibit marked chronicity. We know that chronic appendicitis may exist for many years. The average duration of illness in cases of ulcer operated upon by Mayo²⁹ has been over twelve years. The symptoms of all three affections exhibit marked tendencies to subside and recur. The clinical findings in the three conditions present such striking similarity that errors in diagnosis are frequent.

The age incidence of the occurrence of appendicitis, bile-tract disease, and pyloric ulcer is exceedingly suggestive. The average age at which patients go to operation for chronic appendicitis is twenty-five years; for pyloric spasm, thirty-four years; for bile-tract disease, with or without stones, thirty-nine years; for duodenal ulcer, forty-one years; for gastric ulcer, forty-eight years (MacCarty and McGrath).

There is evidence from Cannon³⁰ that whatever may be the remote cause of pyloric spasm the immediate cause of this phenomenon is an irritation of the duodenal side of the pylorus, and clinical evidence is pretty conclusive that this irritation is inflammation.³¹ Perhaps the nausea and vomiting so indicative as "reflex" gastric signs of acute appendicitis are expressive of duodenitis and

²⁷ *Annals of Surgery*, June, 1908.

²⁹ *Boston Med. and Surg. Jour.*, April 6, 1911.

²⁸ *Abst. Prog. Med.*, December, 1911.

³⁰ *Mechanical Factors of Digestion*.

³¹ I shall in the near future refer to pylorospasm in more detail and more specifically.

its attendant pyloric spasm. This view is in strict conformity to the "law of the intestine," whereby irritation of the bowel causes contraction above the site of irritation. Following the pain as do the gastric symptoms of appendicitis, there is time for the infection and irritative toxic material to pass through the portal vein and liver, to be eliminated by the bile into the proximal duodenum, there to be retained, and cause irritation and inflammation, as a result of the retardation of peristalsis demonstrated by Cannon to follow irritation of the cecum. Surgeons have often noticed the prolonged and pernicious vomiting following delayed appendectomy for this type of appendicitis. It may be that ether and the etherizer are less guilty of causing vomiting than is the disease. Perhaps also the "indigestion" coincident with or antecedent to pain in cases of bile-tract infection, as contrasted to the reverse sequence of symptoms in appendicitis, may be referable to the duodenal catarrh, constituting a part of the pathology of bile-tract infection with or without stone. A single attack of uncomplicated acute appendicitis is too transient in duration to be held responsible for the development of chronic ulcer in a healthy pylorus, though acute duodenitis is frequently and easily recognized.

There are clinical differences, especially in the sex incidence of lesions situated within the portal area, which unless carefully scrutinized may lead to erroneous conclusions. When intelligently analyzed, however, the clinical differences do not antagonize the belief in a common etiology of these lesions, but serve useful purposes in several other directions: For example, pyloric ulcer is found on the table more frequently in men than in women, whereas chronic appendicitis and biliary calculi are more common in women. Appendicitis and bile-tract infection are both more frequent than pyloric ulcer. For acute abdominal diseases, barring gynecologic affections, more males than females are operated upon. In females chronic lesions are found more commonly. Pyloric ulcer, even though chronic, must be more constantly and positively painful and productive of acute indigestion than attenuated chronic infections and gall-bladder calculi.

The same can be said of the sex incidence of bile-tract infection with and without stones. So far as the exciting cause of these two pathologic conditions is concerned, both are dependent upon infection. The more chronic the process the more likely there is to be stone. There may be some anatomic and doubtless there is some physiologic reason why women can tolerate infection sufficiently long to cause gallstones more readily than do men. At any rate, we know that more men than women are operated upon specifically for appendicitis, though the chronic disease is found more frequently in women. More men are operated upon for bile-tract disease without stones, while stones are more frequent in women.

More men than women are operated upon for pyloric ulcer, but there is no reason to believe that the bacteria of the duodenum and bile-tract are more numerous or of greater virulence in men than in women. Perhaps our male intolerance to both pain and infection causes us, by driving us to the table, to secure the preventive treatment of at least gallstones and perhaps of the extension of ulcer or its cause from the duodenal to the gastric side of the pylorus.

Any study based on sex incidence of diseases of the digestive apparatus, save those incident or secondary to pregnancy or lesions of the generative organs, gives little or no information as to the specific primary exciting cause. Men, as compared to women, are notoriously intolerant to pain and to infection. Women have both an inherited and an acquired resistance to infection. Phylogenetically we should expect processes of infection and pain to pursue a more mild clinical course, and be more easily resisted by females than by males. Piersol³² found that in women the duodenum is distinctly V-shaped in 53 per cent. of cases, and in men it is V-shaped in only 23 per cent. of cases. The pylorus is commonly located at a higher point in men (Mayo).³³ As to whether or not these factors favor the location of infection and ulcer, remains yet to be determined.

There are anatomic conditions which make possible the belief, which I am about to express for perhaps the first time, that ulcer of the gastric side of the pyloric sphincter is perhaps a later development representing an extension of infection, and that perhaps the lesion begins as an inflammatory process on the duodenal side of this sphincter in the part of least defence, the fundus of the pylorus.

Anatomic conditions in women may or may not be less favorable to the development of ulcer on the duodenal side, but infection may occur, and being resisted and its symptoms borne, may progress through the lymphatic vessels in the mucous and submucous coats of the pylorus to the gastric side of the sphincter, where it is found at a later period on the table or at autopsy. This may account for the older figures from autopsy findings, showing greater frequency of gastric than of duodenal ulcer in women than in men, though doubtless, as Mayo suggests, many cases in reality of duodenal ulcer were called gastric on account of failure accurately to locate the ulcer in relation to the pyloric sphincter. This continuity of lymphatic vessels in the mucous and submucous coats of the duodenum and stomach may also account for those ulcers which are continuous across the sphincter on both sides.

The past few years have been productive of a considerable amount of knowledge concerning the physiology of the organs of digestion. Many facts which have been known for a long time concerning the anatomy, especially of the upper part of the digestive

³² Human Anatomy.

³³ Annals of Surgery, June, 1907.

tube, have been re-impressed upon us and some important additional facts have been brought forth. The interrelation of the various separate portions of the digestive apparatus and the interdependence of function of one part upon other parts, constitutes now an essential part in the comprehension of normal and pathological digestive affairs. Biological considerations harmonize with facts derived from a study of the morphology of the various parts of the digestive apparatus and of the normal function and morbid disturbances of the alimentary tube and its accessory glands.

Carefully collected clinical experience, closely scrutinized in the light of modern knowledge of physiology and form, can clarify and corroborate many hitherto imperfectly comprehended phenomena concerning the interdependence of disease of various parts of the digestive system upon disease in other parts of the same system, and in some cases of parts remote from and of function independent of digestion. It is not sufficient to study isolated individual disease processes, such, for example as gastric ulcer, appendicitis, bile-tract infection, pancreatitis, because we have learned from pathologic research and systematic observation on the operating table and at autopsy that chronic lesions in these parts are frequently associated with some other disease in the same physiologic system, and that many times a group of clinical phenomena will be found upon the table to be dependent upon two or more definite pathologic processes; located in point of distance anywhere from one or more inches to twenty-four feet from each other. A comprehensive study of either the etiology or symptom-complex of gastric and duodenal ulcer implies also a close study of appendicitis, bile-tract infection, pancreatitis, and, incidentally, of the single and entire portions of the whole digestive apparatus. This study must begin with anatomy, including development, form and structure, to be followed by a comprehension of the newer knowledge of physiology, including the chemical and mechanical factors involved, and along the same line must be viewed many facts from many sources concerning the pathology and bacteriology of the entire apparatus in the living.

And, after all, common-sense conclusions must be deduced by the individual himself, guarding carefully against accepting dogmatically the conclusions of other writers and teachers until the details upon which conclusions are based are thoroughly comprehended.

Pilcher,³⁴ in studying 271 cases of achlorhydria gastrica hæmorrhagica, a complex of gastric symptoms usually described as chronic gastritis accompanied by hemorrhage (generally occult), found that in 100 of these cases the underlying primary lesions were foci of infection within the area drained by the portal vein,

³⁴ Jour. Amer. Med. Assoc., November 19, 1910.

36 being appendicitis alone, 12 appendicitis and gall-bladder disease together, 16 gall-bladder and pancreatic disease together, and 32 to bile-tract disease alone, and in only 16 was the stomach alone involved. These cases showed invasion of the stomach by bacteria, round-celled infiltration of the mucous and submucous coats, engorgement of the capillaries and small punctate erosions. He considered the *rationale* in the production of this chronic gastritis, inhibition of hydrochloric acid, invasion of the stomach by pathogenic organisms, and superficial ulceration or erosion of the mucosa.

MacCarty³⁵ has shown that the zone of induration about the ulcerated area is made up of hyperplasia of connective tissue and invasion of leukocytes, and that the raw surface of the ulcer represents the area from which the epithelial tissue has undergone necrosis and been exfoliated. He states that the cause of the initial necrosis of epithelial tissue is unknown. Reasoning from analogy there seems to be no reason for believing that this necrosis should be strikingly different from the necrosis which occurs as a result of inflammation of mucous membrane elsewhere. Certainly, the indurated hyperplasia, with round-celled infiltration about the base of the ulcer, is not unlike the wall of tissue about a tubercle or carbuncle, and the necrosis of the ulcer does not always differ essentially from the area of necrosis in the centre of a tubercle or carbuncle if such a lesion is sectioned and the cut surface washed with a solution of hydrochloric acid or bile and pancreatic juice.

[As a matter of fact, the life history of a gastric ulcer may be pretty definitely stated as one first of infection of the mucous membrane, followed by connective-tissue hyperplasia, round-celled infiltration, and that ulceration is central necrosis incident to anemia produced by hyperplasia, infiltration, and thrombosis constituting the pathology of local inflammation. Many contributing factors, however, must be active for this process to become chronic and produce the indurated lesion of chronic ulcer.

The contents of the stomach in a condition of health and especially toward the end, or between the intervals of digestion, is practically free from bacteria. Bacteria, though sometimes present immediately following a meal in the chyme as it leaves the stomach, are found in increasingly large numbers and varieties proceeding downward until the contents of the small intestine are discharged into the cecum. The comparative sterility of the stomach and upper bowel depends upon the conjunction of several factors—namely, hydrochloric acid and other bactericidal substances in the gastric secretion and succus entericus together with the mechanical action of mucus, peristalsis, and the retarding action of one species of bacteria upon another.³⁶ Even though the stomach

³⁵ Surg., Gyn., and Obst., May, 1910.

³⁶ Harris, Jour. Amer. Med. Assoc., October 12, 1912.

contains a few organisms immediately following deglutition, cleanliness of the mouth, nose, and throat, and feeding of sterile food, will result in a few days in the disappearance of organisms from the gastric contents. And yet even though the stomach be free from pathogenic bacteria in a condition of health, the lower bowel contains myriads of them. The lower ileum and cecum therefore are the sites of habitat for intestinal flora, and the healthy stomach and upper bowel accommodate bacteria only as transient guests. They can never be made to disappear from the lower ileum and cecum. Peristalsis (Katastalsis) from above and antiperistalsis (anastalsis) from below bring bacteria from the entire digestive tube to the cecum. This structure and its attached appendix may quite appropriately be designated the cesspool of the bowel.

In normal healthy adults investigation has shown that in a large proportion of cases the bile is free from bacteria. But in patients who have disturbances present, or in patients who have had typhoid fever, dysentery, or long-continued constipation the bile always contains bacteria.³⁷ So that we must remember that the cecum and ileum always contain bacteria, and in patients who have had intestinal disturbance the bile also contains organisms. The gall-bladder may also quite appropriately be designated the cesspool of the liver. While the bactericidal properties of the normal stomach prevent most organisms from gaining entrance to the bowel from this source, typhoid bacilli, tubercle bacilli, and certain other specific organisms when ingested in large numbers into the stomach of individuals impoverished by gastric or systemic intolerance may pass the pylorus. Yet from the cecum through the portal vein and liver they readily enter the duodenum by way of the bile. We have long ago learned that bile is not an antiseptic, but is actually a good culture medium. Conradi, quoted by McWilliams,³⁸ shows that bile is not only a good culture medium, but believes that when added to blood serum, bile salts form a fixed combination with the opsonins and promptly destroy the bactericidal properties of the blood serum.

The normal living epithelial lining of the intestinal tube resists the passage of bacteria, but this bactericidal property is not possessed by the secretions and extracts of the epithelial cells,³⁹ and areas from which the epithelium has been eroded by inflammation, afford points of easy entrance of bacteria into the radicles of the portal vein. Once within the blood current pathogenic organisms cause lesions anywhere along the course of distribution of the vessels.

Lewis and Rosenow⁴⁰ collected 68 cases of portal thrombosis; 9 were secondary to bile-tract infection, 6 to cancer of the bile

³⁷ Holmes, New York Med. Jour., August 12, 1911.

³⁸ Annals of Surgery, February, 1911.

³⁹ Schultz, Abst. Prog. Med., December, 1910.

⁴⁰ Archives of Internal Med., April, 1 09.

tract, 10 to pancreatic disease, 6 to gangrenous appendix, 6 to infection of the spleen, 1 to infection of the umbilical vein, 1 to inflammatory pelvic disease, and in 3 cases the cause was unknown.

Post-typhoid, appendicular, and amebic abscesses of the liver are well-known examples of portal-vein transmission of infection. J. F. Percy⁴¹ reported a case of recurrent pyloric ulcer which he believed was due to the persistence of a focus of infection within the gall-bladder, and he suggests that a large majority of cases of ulcer have a history of bile tract infection.

A study of convalescent typhoid carriers made by Gould and Qualls⁴² represent that of 6709 cases of typhoid fever, 4.6 per cent. continued to excrete typhoid bacilli for over ten weeks after recovery. Of 431 typhoid carriers, 211 were temporary and 221 were chronic carriers, and in 12 per cent. of the chronic carriers, cholecystitis is present. The temporary carriers are mostly young people, while the chronic carriers are old, middle-aged, and sickly people. This shows that the excretion of the typhoid bacilli may be intermittent, occurring mostly in women, and may last as long as twenty-seven years. Autopsy as well as clinical studies show that the gall-bladder is the breeding-place.

It has been shown by MacLaughlin⁴³ that the organisms of cholera may be similarly carried as in the case of typhoid fever, though for a shorter time. The excretion of cholera vibrio is also intermittent, and 10 per cent. of all cholera carriers show the organisms in the bile tract.

Crowe⁴⁴ long ago showed that after the administration of hexamethylenamin, formaldehyde could be easily and quickly demonstrated in the bile.

Hartwell and Hoguet,⁴⁵ in working on the subject of experimental intestinal obstruction to determine the cause of death, showed that if the dogs lived after experimental intestinal occlusion as long as one hundred days (one case even after fifty-six days) the duodenum showed edema and inflammatory exudation, exfoliation and formation of acute ulcers. If the dogs had been starved seventy-two hours before the operation, ulcer would not be found, even though some of the dogs lived as long as nine days. These results apply to operations high in the intestine. When the operations are so performed as to occlude and hold in a loop the gastric duodenal and pancreatic secretions, invariably the ulcers were found; if, however, the duodenum were anastomosed low down in the bowel so as to give free drainage, ulcers did not occur, and ligation of the pylorus above the common duct, in no case, is ever followed

⁴¹ Jour. Amer. Med. Assoc., April 9, 1910.

⁴² Ibid., February 24, 1912.

⁴³ Boston Med. and Surg. Jour., October 12, 1911.

⁴⁴ Johns Hopkins Hospital Bulletin, 1908; September, 1912.

⁴⁵ AMER. JOUR. MED. SCI., March, 1912.

by ulcer formation. These experiments, apart from the purpose in studying the cause of death after intestinal obstruction show that the cause of duodenal inflammation and ulceration, is to be found in the microorganisms which are discharged into the duodenum through the bile tract.

Harvey Stone's work,⁴⁶ yet to be published, shows even more positively that the bile is a means of transmission of bacteria to the duodenum.

Regardless therefore of the cause of death following intestinal obstruction, these investigations show conclusively that even after ligation of the pylorus, bacteria from an occluded focus of infection in the lower bowel are carried through the liver and eliminated into the duodenum in the bile. Further, it is shown that bacteria cause inflammation followed by ulceration.

In his Mütter lecture, the late A. O. J. Kelly⁴⁷ cited in detail sufficient evidence to show that ascent of infection from the duodenum to the bile tract through the lumen of the duct was imaginable, but that it does not actually occur. It is hard to believe that bacteria from the duodenum are sufficiently vigorous to pass through the minute orifice of the common bile and pancreatic ducts against a stream of bile under a pressure of at least 700 millimeters of water, and then with sufficient intelligence and motive to turn almost invariably to the left and proceed vertically upward in the common duct instead of to the right and horizontally into the pancreatic duct against considerably less pressure and volume of fluid. The fact that bacteria are found in larger numbers near the duodenal end of the duct than at higher points is not proof that they enter from the duodenum. The sphincter about the duodenal orifice of the common duct acts in a manner not unlike that of a dam or jetty in a stream of water; filth and solid particles of all kinds in such a stream tend to accumulate above an obstruction. The fact also that the bacteria in the lower end of the common duct are found in greater numbers than in the gall-bladder fails also to prove that they are actually present in greater numbers. On account of the greater quantity of fluid bile in the gall-bladder the bacteria are in greater dilution than in the common duct, and we would expect to find relatively fewer bacteria in a given quantity of gall-bladder contents examined than would be found in a similar quantity of the contents of the common duct.

Small particles of indigo coloring matter placed in the rectum have been recovered from the higher portions of the small intestine. Bond⁴⁸ has apparently demonstrated that small particles may be conveyed along a mucous canal in a direction reverse to that of the normal contents of the tube, provided that the tube be suffi-

⁴⁶ Medical Society of Virginia, 1912.

⁴⁷ AMER. JOUR. MED. SCI., September, 1906.

⁴⁸ Quoted by Kelly, *loc. cit.*

ciently nearly empty as to permit partial or complete apposition of its walls. It is doubtful if the gall-bladder and common duct are ever under any circumstances sufficiently nearly empty as to permit apposition of its walls. On the contrary, the bile tract has no adequate expulsive mechanism other than the pressure caused by the volume of its contained bile, and this must amount to 700 millimeters of water to overcome the resistance offered by the sphincter about the orifice of the common duct. Indeed, this overdistention is believed to be the cause of the formation of that diverticulum of the common duct which we have designated gall-bladder. Anatomists dispute the presence of muscular tissue in this structure and no one has ever seen the gall-bladder exhibit muscular contraction. As a matter of fact there is sufficient experimental evidence from many sources that ascending infection in the sense of transmission of infection, along the lumen of any canal against the current of the physiologic excretion, does not occur. The experiments in this line have been carried out chiefly with reference to the urinary organs, though the deductions have general application.

Many cases of pancreatitis, acute and chronic, are associated with pyloric ulcer, and this has contributed to the belief formerly held by many, that infections of the pancreas were commonly the result of ascending infection from the duodenum to the pancreas by way of the pancreatic duct. Since pancreatic infection has been recognized as secondary to bile-tract infection, and since as we are about to recognize that duodenal infection is also a result of the infection in filthy bile, there is ample reason to acknowledge the justifiable association of pancreatitis and pyloric (duodenal) ulcer. Many cases of inflammation in and about the head of the pancreas are believed, upon the basis of recent studies of the lymphatics in this region, to be in reality peripancreatic lymphangitis rather than true pancreatitis. There can be no question, however, that the substance of the gland does actually become infected through regurgitation of infected bile upon the pancreatic duct when the duodenal end of the common duct is blocked by gall-stone impaction, in a manner identical with the development of liver abscess upon common-duct impaction. This is not ascending infection, but retention of infection.

There are even yet a few who seem to believe that infection may be conveyed to an organ from remote sources through the lymphatics. So far as I can learn no one has demonstrated the occurrence of backward flow in lymph channels, and unless this can happen extension to an organ of infection through lymph vessels is an anatomic impossibility. Lymphatics lead from and not into organs. The lacteals from the bowel certainly absorb and transmit food, filth, and other substances to the mesenteric lymph node filters, from which the venous radicles in and about these structures

rapidly convey to the liver the food for further assimilation and the infection and filth for destruction. It is true that lymphatic vessels in the immediate vicinity of the pylorus, under surface of the liver, and pancreas by their generous anastomosis perhaps permit of mixing of lymph from one area with that from another area. Thus peripancrreatitis, perihepatitis, and periduodenitis may arise. But the lymph current is always from the interior of every organ to the thoracic and right lymphatic ducts which empty into the subclavian veins.

With reference to transmission of infection from the duodenum to the bile tract we must remember that, save when diseased, the duodenum is not the habitat of bacteria, and even when in rare cases a few may be found, they are regarded as transients on a rapid journey to the cecum. On the other hand, when the duodenum is infected the bacteria are abundant, and the belief of all observers, and the bacteriologic observations of Pilcher⁴⁹ indicate that duodenal infection is generally secondary to foci of infection in the bile tract or bowel. In reality the liver is a vital repository for food and filth brought from the entire bowel by the portal vein, the food to be prepared for assimilation and appropriation by the economy, and the filth to be filtered and partially or completely destroyed. The residue mixed with certain specific substances perhaps manufactured in the liver, drains through a system of sewers, the bile tract, into the bowel, there to serve purposes doubtless useful to the economy, though when virulently or constantly polluted, to spread and under certain circumstances to plant infection. Thus is established a vicious circle made of links of infection difficult to destroy. And even though many partially or completely obliterated appendices are found upon examination to be at the moment free from bacteria, it will scarcely be questioned that through the areas from which the bactericidal epithelium has been eroded, bacteria and poisons from the cecum may enter the portal radicles, and that the ileocecal stasis incident to the irritation of the diseased appendix is favorable to absorption of filthy bowel contents.

"Oral sepsis" has been assigned as the source of infection for gastric ulcer. Türk⁵⁰ after feeding dogs for three or four months on large doses of filth made up of boullion and culture of colon bacilli, succeeded in producing acute ulcer of the stomach and the duodenum, but upon a cessation of the feeding the ulcers healed. Feeding in somewhat smaller quantities and over a long time, he succeeded in producing an ulcer which resembled the chronic ulcer in man, but was in reality somewhat different in pathology.

This seems to be the nearest approach to chronic ulcer ever produced experimentally. And the nearest clinical approach to

⁴⁹ Loc. cit.

⁵⁰ Abst. Prog. Med., December, 1910.

this experimental cause to be found in the human being is perhaps the constant feeding through the bile tract of colon bacilli and other pathogenic bacteria from a focus of chronic recurrent infection in the area of bowel drained by the portal vein. Such individuals may be as dangerous to themselves as are chronic typhoid carriers to the community.

Not only is infection more constantly and in more virulent form and larger dosage brought from foci within the portal area to be deposited into the proximal duodenum or fundus of the pylorus by the bile, but the virulence of the bacteria fails to be attenuated by hydrochloric acid, as they would be if swallowed, and the delayed and enfeebled peristalsis incident to irritative inflammatory lesions low down in the bowel, favors retention in the duodenal part of the pyloric region (another cesspool) and delays the discharge of bactericidal acid from the stomach (Cannon). Thus proximal duodenitis (pyloritis) results, causing immediate pyloric spasm, and the process of inflammatory ulceration is begun. Such a route of infection, from bowel sepsis, seems at least more reasonable and clinical than the belief held by many of ulcer secondary to the oral sepsis incident to decayed teeth, tonsillitis, gingivitis, and the like.

There are several important considerations with reference to the anatomy and physiology of the stomach and duodenum in relation to ulcer. The point of the duodenum above the common duct—namely, about the first four inches—is in reality a part of the stomach, and should so be considered. This part of the alimentary tube together with the stomach proper is derived from the foregut; has the same blood supply as the rest of the stomach—namely, through the celiac axis; the same nerve supply through the pneumogastrics and sympathetics, and the same lymphatic drainage. Its mucous membrane is thin and granular, it contains no valvulæ conniventes, and does contain Brunner's glands, which are identical in structure with the hydrochloric-acid glands of the stomach. Its functions and diseases are those of the pyloric region of the stomach. The proximal duodenum does not exhibit peristalsis, and in this respect is like the cardiac end of the stomach. Like the cardiac end also it serves as a mixing chamber for the food and digestive secretions. It is acted upon by respiratory movements of the diaphragm through the liver, and like the cardiac fundus has muscular tone of its own.

A new nomenclature might designate various parts of the stomach as follows: It is divided into two parts, the left or cardiac portion and the right or pyloric portion, by a line passing from the incisura angularis on the lesser curvature to a point opposite on the greater curvature. The cardiac portion would then be subdivided into the cardiac fundus, sac, or chamber, and the body of the stomach; and the pyloric portion would be subdivided into the pyloric ves-

tibule, pyloric canal, and pyloric fundus, sac, or chamber, at present designated as the proximal duodenum (Mayo).⁵¹

The fundus and body of the stomach are supplied by the gastric and splenic arteries, while the whole pyloric portion, including the pyloric chamber down to the common duct, is supplied by the hepatic artery through its pyloric and gastroduodenal branches. The small intestine beyond the common duct gets all of its blood supply through the superior mesenteric arteries, and even the inferior pancreaticoduodenal branches of this vessel does not supply any part above the common duct. The veins all empty into the portal.

The entire pylorus and duodenum when considered together are arranged grossly in the shape of an "S" placed transversely. This shape is comparable with that of the S-trap employed by plumbers, and allows the acid chyme, bile, and pancreatic fluid to accumulate in the pylorus between the sphincter muscle and the common duct. That accumulation actually occurs is shown by the fact that this part of the pylorus is always stained with bile after death, and in comparison with the remaining part of the small intestines is much dilated. X-ray pictures taken after administration of bismuth show an accumulation of bismuth in this part of the "pyloric cap." The S-shaped arrangement also prevents regurgitation of gas and fluid from the small intestine into the stomach.

The upper margin of the entire stomach along the lesser curvature and for two inches beyond the pyloric sphincter is suspended from the liver by the gastrohepatic omentum (the free edge of which is called the duodenohepatic ligament), and allows free mobility of the stomach and proximal duodenum. Beyond the duodenohepatic ligament, and especially beyond the opening of the common duct, the duodenum is securely fixed in position, behind the peritoneum.

Chronic ulcers of the pyloric region are found just twice as commonly in that portion just distal to the pyloric sphincter as they are in the part of the stomach on the proximal side of the sphincter. In 621 cases Mayo⁵² found 64.5 per cent. on the duodenal side and 32.5 per cent. on the gastric side of the pyloric sphincter; 3 per cent. were found on both sides. Seventy-five per cent. of his cases occurred in men. By all odds the greatest number (90 per cent.) of ulcers are found in the first two inches of the duodenal portion of the pylorus, and there are definite anatomic reasons why this should be so. This location corresponds to the highest point of the pyloric region, the fundus. The fundus of all organs is generally deficient in blood supply as compared to other parts of the organ.

⁵¹ Surg., Gyn., and Obst., June, 1908.

⁵² Loc. cit.

Witness for example the gall-bladder, the urinary bladder, the uterus, and even the fundus of the cardiac end of the stomach. Mayo's anemic spot⁵³ is located in the fundus of the pylorus, and Wilkie,⁵⁴ from a study of 40 specimens, with reference to the arterial supply of the pyloric area, found the first two inches of the duodenal portion of the pylorus markedly deficient in blood supply as compared with the rest of the region. This first two inches is supplied by the supraduodenal artery, which, though usually a branch of the gastroduodenal, sometimes arises from the hepatic and other arteries in the neighborhood. The anastomosis of the supraduodenal with the surrounding arteries is imperfect, and often the supraduodenal is a true end artery with no anastomosis. The first two inches of the duodenal portion of the pylorus is therefore designated as the critical area on account of its deficiency of blood supply and its well-known common seat for ulcer formation. The dome of this region is commonly the point affected, and the dome of all hollow organs is relatively poorly supplied with blood. The slight local anemia incident to vascular sclerosis may account for the greater tendency to ulcer in men as compared to women. Ulcer is in reality local circumscribed gangrene, and men are more frequently the victims of gangrene than are women, though no more commonly the soil for infection.

Moreover, the first two inches of the pyloric part of the proximal duodenum is freely movable, whereas the area beyond is comparatively fixed. It therefore represents the junction of a fixed and movable portion. The tendency for infection to be located at such a junction is strikingly manifested by the localization of tuberculosis of the spine at the dorsolumbar junction. Moreover, in the pylorus this area represents the junction of two curves—namely, the ascending and the descending portions of the proximal duodenum. The tendency for localization of tuberculosis of the spine at the meeting-place of two curves is also conspicuous, and this tendency is exhibited by other structures throughout the body.

Finally, with some reservation, I would submit for discussion the following opinion:

1. The actual pathology of pyloric ulcer is that of central necrosis of an area of inflammation, the necrosis resulting from capillary and arterial blocking by hyperplastic connective tissue and inflammatory exudate.
2. The exciting cause of the inflammation causing the necrosis is bacterial infection.
3. The original source of the bacteria is from some focus of inflammation in that part of the body drained by the portal vein—

⁵³ Loc. cit.

⁵⁴ Wilkie, Surg., Gyn., and Obst., October, 1911.

namely, the small intestine, appendix, cecum, colon, sigmoid, upper part of the rectum, liver, bile tract, pancreas, and finally the stomach itself.

4. The bacteria are carried to the liver through the portal vein.

5. The bacteria are eliminated in the bile after being filtered through the liver.

6. The infection is deposited by the bile into the proximal duodenum or according to the new nomenclature, pyloric fundus, sac, or chamber.

7. The clinical phenomena of pyloric spasm are dependent upon the pathology of duodenal pyloritis.

8. Pyloritis, pyloric ulcer, bile-tract infection, pancreatitis, and perhaps cirrhosis of the liver are late results of infection primarily located most commonly in the appendix, though in many cases in some other region drained by the portal vein; and these lesions frequently exist together in the same patient at the same time or may follow each other in rapid or slow succession.

9. That the cause of pyloric ulcer (inflammation) is probably always primarily located on the duodenal side, and that so-called gastric ulcers are a result of extension of infection from the duodenal, through the lymph vessels in the wall of the pylorus to the gastric side.

REVIEWS

A MANUAL OF SURGICAL TREATMENT. By SIR W. WATSON CHEYNE, Bart., C.B., D.Sc., LL.D., F.R.C.S., F.R.S., Hon. Surgeon in Ordinary to H. M. the King, Senior Surgeon to King's College Hospital; and F. F. BURGHARD, M.S. (Lond.), F.R.C.S., Surgeon to King's College Hospital, and Senior Surgeon to The Children's Hospital, Paddington Green. New edition, entirely revised and largely rewritten with the assistance of T. P. LEGG, M.S. (Lond.), F.R.C.S., Surgeon to the Royal Free Hospital, Assistant Surgeon to King's College Hospital; and ARTHUR EDMUNDS, M.S. (Lond.), F.R.C.S., Surgeon to the Great Northern Central Hospital, and Surgeon to Out-Patients, The Children's Hospital, Paddington Green. In five volumes. Vol. III, pp. 575, 271 illustrations; Vol. IV, pp. 622, 208 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THE first and second volumes of this revised edition of Cheyne and Burghard's popular *Manual of Surgical Treatment* were reviewed in the pages of this JOURNAL in November, 1912. The third and fourth volumes appeared early in the present year. They include the treatment of surgical affections of the joints, head, face, and spine (Vol. III), and of the tongue, mouth, pharynx, esophagus, stomach, intestines, rectum, and anus (Vol. IV).

The section of Volume III dealing with affections of the joints covers first injuries, which includes dislocations and wounds, and secondly joint diseases. The first chapter in the latter section includes acute inflammation (acute synovitis, acute suppurative arthritis, gonococcal arthritis, pneumococcal arthritis, etc.), and chronic inflammation (chronic synovitis (*a*) with effusion, and (*b*) with synovial thickening); then follow separate chapters on tuberculosis and syphilis of joints, nervous affections of joints, rheumatoid arthritis, loose bodies in joints, and ankylosis. This skilfully evades the vexed question of the classification of some of the latter affections. Most of the subjects are discussed in sufficient detail, and the treatment recommended is that which experience has proved the best; but in the case of suppurative arthritis it surely would have been well to include among recognized methods of treatment weight extension, as well perhaps as formalin-glycerin injections. In the treatment of Charcot joints the authors recommend arthrotomy and drainage in the early stages, to be followed by the use of a brace until death. Excision is condemned.

Under the heading Acute Rheumatoid Arthritis they discuss with somewhat excessive brevity the affection now commonly known as atrophic arthritis; and as Chronic or Monarticular Rheumatoid Arthritis or Osteo-arthritis a fairly satisfactory account is given of what is generally called hypertrophic arthritis. When the latter affects the hip they rightly say that excision is of no use, "giving extremely bad functional result," but they seem not to be familiar with Albee's method of arthrodesis, as they probably would approve it if they ever heard of it, since they commend excision of the knee because it produces ankylosis.

The general subject of ankylosis is discussed in three pages, and a cursory description is given of arthroplasty, with illustrations of Murphy's operation on the hip; but the authors seem to have no personal familiarity with the method as applied to any joint. Then follow chapters on affections of special joints. A curious contradiction is found in the chapter on tuberculosis of the hip-joint: the authors state that the disease is practically never cured, and warn against any active interference even after many years of apparent recovery (p. 127), yet at p. 180 advise arthroplasty "when the disease has passed off completely," whatever that phrase may mean. In spite of this advice, which seems injudiciously radical, there is no mention of Albee's operation for ankylosing the spine, which though radical in one sense is in another sense most truly conservative, because the best and surest "cure" for tuberculous arthritis anywhere in the body is the occurrence of bony ankylosis.

The remainder of the volume, devoted to the surgery of the head and face, calls for no special comment. The various operations (brain, cranial nerves, face, palate, lips, etc.) are adequately described and illustrated by excellent figures.

Volume IV covers the treatment of the alimentary canal from mouth to anus. In treating fractures of the mandible the usual modern preference is given to dental appliances, the authors especially commending Hammond's interdental wire splint, which should be applied (under a general anesthetic) by a competent dentist. Lilienthal's operation for ankylosis of the mandible is better than the methods here described for this serious condition.

In discussing tumors of the jaws, the advice is given to enucleate the eye at once whenever the orbital plate has to be removed in excision of the upper jaw, even if the eye is not diseased, because they consider that the disability from the diplopia which may result if the eye remains is so great as to demand this treatment subsequently in all cases. In connection with various operations on the mouth Dr. Silk describes venous anesthesia, and the method of intratracheal insufflation, whose introduction he attributes to "Metzler" of the Rockefeller "Institution," but with which none of the various authors appears to have any personal familiarity.

Cheyne and Burghard prefer to give the anesthetic through a laryngotomy opening.

In operations for carcinoma of the tongue it is recommended that the lymphatics and the tongue be removed at the same time unless the wounds will have to be made to communicate; in the latter case they think the lymph nodes should be removed first.

Discussing the treatment of wounds of the stomach they urge mopping out the abdomen and then irrigation to remove the extravasated gastric contents, and evisceration if there are foreign bodies (pieces of potato, etc.) in the abdominal cavity. It seems questionable, however, whether such prolongation of the operation does not do more harm than allowing food particles, which after all have been sterilized by cooking, to remain. Likewise, in the operation for intestinal obstruction they advise allowing the prolapse of all bowels which tend to prolapse, so soon as the abdomen is opened. "It is becoming a favorite practice," they add, "to receive the protruded coils into hot cloths smeared with sterilized vaseline or pure paraffin in order to avoid damage to the epithelial coat;" and they speak favorably of the use of a glass tube to evacuate the distended bowels by the method of Monks (pushing coil after coil over the glass tube). The former practice seems less calculated to prevent injury to the serous coat of the bowels than the method of keeping them all in the abdomen whenever possible (and it is usually possible), and the plan of Monks, though seductive in theory and attractive in half-tone illustrations, has not much to commend it in actual practice.

The concluding portions of the volume, which deal with ulcers and tumors of the gastro-intestinal tract, with hernia, and with appendicitis, are well presented and freely illustrated. Even though English surgeons have at last adopted American indications for operation in cases of appendicitis, it is strange that they have still so much to learn from this side of the water in regard to the technique of the operation.

The fifth and last volume, which should shortly make its appearance, is to contain the surgery of the upper abdomen and genito-urinary surgery, as well as that of the neck, the thorax, and the breast.

A. P. C. A.

THE NARCOTIC DRUG DISEASES AND ALLIED AILMENTS. By GEORGE E. PETTEY, M.D., Member of the American Society for the Study of Alcoholic and Narcotic Diseases, of the American Medical Association, etc. Pp. 516. Philadelphia: F. A. Davis Company, 1913.

THIS volume contains 26 chapters of which 20 including quotations are devoted to morphinism. The author deprecates the word

"morphinism" and prefers that of "narcotic addiction," which should meet with general approval. Further, he considers it a disease and not a habit, a toxemia of drug, auto, and intestinal origin belonging to the field of medicine and not neurology. The use or rather the misuse of the hypodermic syringe is held responsible for the alarming increase of cases of morphine addiction in the last forty years. At this point may be mentioned a valuable practical fact evolved from the experience of the author that "in the average Caucasian, thirty days daily use of morphine is enough to establish the 'addiction' to such a degree that very few persons would be able to extricate themselves from it by their own efforts."

Consistently with his belief that the disease is purely and solely a toxemia, he claims that if every cell and structure of the patient's body can be freed from toxic matter there will be no nervous manifestation or suffering incident to the withdrawal of the narcotic. The successive doses of the drug imperfectly eliminated, tend each time to promote its accumulation in the tissues. To the drug, however, are added other waste products whose elimination is suppressed by its presence and to these more than to the narcotic itself the author assigns the symptoms and complications met on its withdrawal, these symptoms being held in abeyance during its administration. Elimination is therefore the keynote of treatment. To this end the bowels and kidneys are availed of, the former with a view more especially to promoting biliary secretion and relieving portal congestion. The administration of purgatives is, moreover, preceded by full doses of strychnin to stimulate the unstriated muscular fibers of the intestine before the centres governing voluntary motion are materially affected. Calomel, cascara, rhubarb, and castor oil as determined by circumstances are purgatives mentioned as meeting the indication, but calomel especially.

The author does not approve of the gradual withdrawal of the drug, saying that "it is as unreasonable and unscientific as unsuccessful." On the other hand he says also the abrupt withdrawal of an opiate from a person addicted to its use without preparing his system for it is not only dangerous to life but it is barbarous. This statement seems somewhat contradictory, but he says also that such danger is, however, obviated if a proper course of preparatory treatment is carried out, namely the eliminative and the "cleansing" treatment above referred to. The purgative treatment is started about 4 P. M. and the last dose given at about 10 P. M. At first the opiate is kept up in the usual doses but none given after 8 or 10 P. M., until after the bowels are moved the following morning. It is again briefly returned to under certain conditions, in much smaller doses which are found to be equally efficient. This would appear to us somewhat of the nature of gradual withdrawal of which he says he does not approve. Chiefly, however, the patient's suffering is subdued by the discrete administration of scopolamine

(hyoscine) in such doses as are necessary to overcome all painful symptoms and to keep the patient comfortable, the dose being $\frac{1}{300}$ to $\frac{1}{50}$ grain as required by the individual case.

"Alcohol in all forms should be interdicted during the convalescence and forever afterward," but institutional treatment, strychnine in large doses to excite the motor function of the bowel, liberal diet and narcotics other than scopolamine are used as adjuvants. Among the narcotic adjuvants employed are atropin, daturin, gelseminin, pilocarpin, and aspirin. Elimination, judicious withdrawal of the drug, control of withdrawal symptoms by scopolamin and other narcotics, support by liberal diet and strychnin are the agents for the details of whose use the reader is referred to the book.

Other subjects treated are the cocaine habit, chronic alcoholism, delirium tremens as well as the acute ailments occurring in persons addicted to the habitual use of narcotic drugs.

Much interesting and valuable information in the shape of quotations from the literature on "opium addiction" and on collateral matters is contained in the book which makes it interesting reading. Not the least of these are extracts from De Quincy's "Confessions of an Opium Eater, his "Pleasures and Pains of Opium" and other essays. Most of the generation which read these interesting papers when published in the "fifties" and earlier, during the height of De Quincy's popularity have passed away and there are perhaps few living who are familiar with them. Notwithstanding the mischief they may have done at the date of their publication in suggesting the use of opium for the sake of the pleasure pictures which De Quincy drew, they should be read as representing the classics of a brilliant period in the history of English literature, covering that part of the Victorian age from 1837 to 1859, in which De Quincy's "faultless refinement of style" and "marvellous mastery of phrase" played a conspicuous role.

J. T.

ORGANIC AND FUNCTIONAL NERVOUS DISEASES. A TEXT-BOOK OF NEUROLOGY. By M. ALLEN STARR, M.D., PH.D., LL.D., Sc.D., Professor of Neurology, College of Physicians and Surgeons, New York. Fourth edition. Pp. 970; 323 engravings and 30 plates. Philadelphia and New York: Lea & Febiger, 1913.

WHEN Dr. Starr's work first appeared, it was as a treatise on organic nervous diseases, but all subsequent issues have included functional disorders and it is in the latter section that most of the new matter has been inserted. In the preface of this edition it is stated that chapters are added on symmetrical gangrene and

angioneurotic edema. There are still some diseases which we feel might with advantage be included and among these are exophthalmic goitre and acromegaly; such diseases appear as worthy of consideration here as does paresis.

The chapter on brain tumors has been rewritten and considerable new matter is presented. Chloroma is discussed and a patient with such a tumor in whom both optic nerves, one sixth nerve, both glossopharyngeal nerves and one hypoglossal nerve were paralyzed was seen by the author. Tumors of the cerebellopontine angle are given much more consideration than formerly and the symptoms are divided into three classes: (1) Those referable to the cranial nerves; (2) those referable to the involvement of the cerebellar peduncles; (3) those referable to compression of the tracts passing through the pons.

Pellagra has been included and headache and the disorders of sleep have been given separate consideration.

The chapter on epilepsy remains unchanged. We do not agree with the author in the prominence given alcohol as a cause of epilepsy. Even in parents, the nervous instability which drives them to drink may in part be responsible for the development of epilepsy in the child. The report of the Craig Colony for 1912 gives alcoholism as the probable cause in less than one per cent. of the admissions for that year. We know that drinking is very common and epilepsy is relatively rare; alcoholism is much more common among males while epilepsy is at least as common among females; many cases of epilepsy have developed before the age when drink could be obtained; and even those drinkers who have convulsions (so-called acute alcoholic epilepsy) seldom have fits independent of their drinking.

The most notable addition to the book is in the chapter on hysteria. Of the theories of this disease, those of Babinsky, Janet and Freud are briefly set forth. As to Freud's hypothesis, elements of truth are admitted, but its many errors call forth sharp criticism from the writer, which in the main is, that the method is most limited in its scope and has many objectionable features not shared by the direct persuasion of Babinsky or the hypnosis of Janet.

This volume is by no means a compilation. It is announced in the foreword that the author has drawn many definite conclusions from the mass of pathological and clinical material that has accumulated in the thirty years' practice of his specialty, and this statement is well borne out in the text. The book bears more of the imprint of the personal observation of its author than any neurology that has yet appeared by an American writer, and this feature accords it a most welcome place in the library of the neurologist. It is, furthermore, a most excellent work for the student and practitioner.

N. S. Y.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Volume II: February, pp. 179, 32 illustrations; April, pp. 174, 35 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THE first number of the second volume of Murphy's Clinics opens with an interesting address by Mr. W. Arbuthnot Lane, of London, on the open treatment of fractures. This is a written address, carefully prepared, and read at Dr. Murphy's clinic, November 23, 1912. In it Mr. Lane reviews his work in the operative treatment of fractures from its inception over twenty years ago to the present time. He says "till surgeons generally have improved their technique sufficiently, and have acquired a greater familiarity with the operative treatment of fractures, a varying degree of risk must necessarily accompany any open operation, and this danger has to be taken into consideration." After urging the importance of skiagraphs in determining for or against immediate operation, he recommends that, whatever course of treatment is decided on, it is advisable "to obtain a written and witnessed acquiescence, so as to secure the medical attendant from subsequent loss, annoyance, and anxiety." He proceeds: "to trust entirely to the now practically obsolete symptom called crepitus, and to an imaginary familiarity with the other clinical symptoms of fracture, is absurd in the present day, when every detail of any importance can be learnt by means of radiography, which is perfectly reliable in competent hands." Evidently he must think a great deal of time is wasted in most medical schools in teaching students how to reach a diagnosis in cases of suspected fracture. How much simpler to let the Professor of Röntgenology conduct all the instruction in fractures, and for the country doctor to send every patient who sustains any injury whatever to any of his limbs, to the nearest city, perhaps fifty or a hundred miles distant, for radiographic examination, in order to ascertain whether or not a fracture is present. Not only this, but, according to Mr. Lane's standard, it is perfectly unjustifiable at the present day for any one but a competent and *experienced* "bone surgeon" to undertake the treatment of any fracture.

Another interesting address in this same number is that by Dr. W. C. Woodward, Health Officer of the District of Columbia, on the "Medico-legal Relations of Physician and Patient."

In addition to these more or less formal addresses there is the usual abundant supply of clinical material discussed entertainingly and instructively by Dr. Murphy himself: this includes osteitis of the femur; floating cartilages in the knee; fecal fistula following appendectomy; tuberculosis of the knee; amputation of the breast for Paget's disease; pyosalpinx; cerebral decompression; laminectomy for paraplegia; congenital pyloric stenosis and hour-glass stomach. The value of these clinics is materially

enhanced by the diagnostic acumen of Dr. C. L. Mix, who is almost constantly present to comment on aspects of the cases which are not purely surgical.

The second number, that for April, is largely devoted to abdominal lesions. Noteworthy is the address by Mr. Robert Milne, of the London Hospital, on certain aspects of gastric ulcer. He says: "In the mucous membrane of the stomach, and even partially in the submucous coat, there are small collections of lymphoid tissue. These are in greatest number along the lesser curvature and in the prepyloric region of the stomach; rare in the cardiac portion. Although small in a healthy stomach, when inflamed they swell up, push the mucous glands apart to each side, and reach the surface." From this point on the pathogenesis of gastric ulcer is largely conjectural; he conjectures that if suppuration occurs in these lymph follicles and that if they burst into the gastric cavity, then the gastric juice is allowed to enter, digests the coat of the stomach, and thus may lead either to the acute perforating ulcer or to the chronic ulcer and so to carcinoma. On the other hand, ulceration into a bloodvessel may occur, and in this way he conjectures hemorrhagic erosions arise. He further discusses in an interesting manner the modern theories as to the pathogenesis of gallstones and renal calculus.

Dr. Murphy's reported operations and clinical lectures include: hysterectomy for "essential hemorrhage" of the uterus; a number of upper abdominal cases; cases of intestinal surgery (adhesions, short-circuiting, etc.); spina bifida; laminectomy for fracture of the spine, with discussion of the neurological aspects of the case by Dr. Peter Bassoe; a case of ureteral calculus; one of cerebellar tumor with subtentorial decompression; transplantation of bone for necrosis of the tibia; plating a fracture of the leg (operation by Dr. Philip H. Kreuscher); amputation for periosteal sarcoma of the thigh; as well as other topics too numerous to mention.

This volume gives evidence so far of more careful preparation than the earlier numbers of Volume I; and from the editor's note at page 242 it appears that the editor is Dr. Murphy himself. Some pages of the April number have a faint smell of the lamp about them; but for educational purposes this steadier light is perhaps preferable to the sparks and flashes which were so abundant at first.

A. P. C. A.

STUDIES IN SMALLPOX AND VACCINATION. By WILLIAM HANNA, M.A., M.D., D.P.H., Assistant Medical Officer of Health of the Port of Liverpool and Visiting Physician to the Port Isolation Hospital. New York: William Wood & Company, 1913.

THE author presents a monograph of 52 pages containing 24 full-page halftone illustrations devoted to the influence of vacci-

nation as based on an analysis of 1163 smallpox cases observed by him in the city and port of Liverpool.

Among 943 cases of smallpox vaccinated in infancy, there were 28 deaths, or 2.9 per cent., while among 220 unvaccinated, there were 60 deaths, or 27.2 per cent.; the ratio of deaths to attacks was ten times as great in the unvaccinated as in the vaccinated. These figures are, in a general way, confirmatory of the common experience of smallpox hospitals as to the lifesaving influence of vaccination.

The opponents of vaccination, in order to discredit the statistics of smallpox hospitals, are forced to charge, as they virtually do, a world wide and century long conspiracy among the officers of these institutions to falsify the classification of the vaccinated and unvaccinated groups. The charge is that being in favor of vaccination, the physicians are so biased that their observations are worthless. If the observations of men of vast experience in smallpox are worthless, what can be said of the observations of the paper statisticians opposed to vaccination.

Dr. Hanna makes an interesting contribution to the study of the mutual influence of concurrent vaccinia and smallpox in cases in which vaccination was performed during the period of variolous incubation. In consonance with the views of others, he finds that a vaccination performed subsequent to infection with smallpox, will "take" and pass through its typical course, up to the date of onset of symptoms of smallpox.

The chances of suppression or favorable modification of the oncoming smallpox, are in inverse ratio to the period elapsing between smallpox infection and vaccination; the later the smallpox appears after vaccination, the greater is the opportunity for the vaccination to be successful and develop its counteracting immunity. The author states that "vaccination requires nine days to develop an immunity which will absolutely prevent or minimize an attack of smallpox."

The author makes some interesting observations on the question of vaccination after the onset of smallpox. "The operations performed subsequent to the onset of symptoms were unsuccessful." He believes, however, that in some cases the vaccine organisms introduced into the system may have had some modifying effect, although the reaction was not typical.

In cases vaccinated late in the course of the disease, no reaction appeared at the site, except of course the usual scarification crust. An erroneous judgment may be reached through confusing the increased variolous eruption about the vaccination site as the effect of vaccination.

The little volume contains an illuminating series of well-executed photographs showing concurrent vaccination and variola. The monograph will prove of particular value to vaccine physicians, health officers, and others specially interested in the subject.

J. F. S.

FURTHER RESEARCHES INTO INDUCED CELL REPRODUCTION AND CANCER. Consisting of papers by H. C. ROSS, J. W. CROPPER, and E. H. ROSS. Vol. II. Pp. 120; 9 illustrations. London and Philadelphia: John Murray and P. Blakiston's Son & Co., 1912.

THE work described in this book is a continuation of earlier work on the same general subject. Among other things, the workers claim to have produced swellings resembling tumors in experiment animals. They have used the same general methods as Leo Loeb and as Stoeber and Wacker, and have reached the same results, but the descriptions of experiments and results leave much to be desired in conciseness and accuracy of statement, so that the reader has difficulty in reaching a definite conclusion.

The writers claim to have induced division of trypanosomes, but although the studies are of some interest, they are by no means conclusive. E. H. Ross has worked out the development of the leukocytozoön of the guinea-pig (Kurloff), but no very definite conclusions are drawn. J. G. Thomson has prepared an extremely concise and clear description of a spirochete found in the feces of the guinea-pig.

It is difficult to comment on the book as a whole because for the most part it is no more than an amplification of statements made in the preceding volumes. It may be said, however, that the reviewer finds no more conviction in this book than in the others and sees little reason for its publication. H. T. K.

PHYSICAL DIAGNOSIS. By RICHARD C. CABOT, M.D., Assistant Professor of Medicine in the Harvard Medical School, Boston. Fifth edition. Pp. 519; 5 plates and 268 figures in the text. New York: William Wood & Co., 1912.

A BOOK which has reached its fifth edition in seven years (the fourth in 1909) like good wine "needs no bush." It is for the most part sufficient, therefore, to note the chief changes which have been made to bring it up-to-date. They include sections on the phlebogram, the arteriogram, the recasting of the section on blood pressure and the arrhythmias, on subphrenic abscess and peptic ulcer. The section on bismuth x-ray examination of the stomach is also enlarged. Dr. Cabot's characteristic incisive style marks the book throughout and increases its attractiveness. It is at once a book of reference and a reliable source of information helpful to a correct diagnosis, the essential basis of a correct treatment. We know of no book on the subject which is more

accurate in its descriptions and more reliable in its statements. Its size, midway between the brief compend and the unwieldy heavy volumes so often met, is a quality which contributes to the convenience and facility in handling so necessary to the greatest availability of a book.

J. T.

PRINCIPLES OF HYGIENE, AND PRACTICAL MANUAL FOR STUDENTS, PHYSICIANS, AND HEALTH OFFICERS. By D. H. BERGEY, A.M., M.D., First Assistant, Laboratory of Hygiene, and Assistant Professor of Bacteriology, University of Pennsylvania. Fourth edition. Philadelphia and London: W. B. Saunders Company, 1912.

THE previous editions of Dr. Bergey's *Principles of Hygiene* have had a very wide distribution, and have been well received by workers in this field. The present edition promises to keep up this reputation. The great advancement in our knowledge concerning the methods of causation and prevention of disease has made necessary rather rapid revision of works on hygiene. The book under discussion has been brought up to the latest ideas in the subjects treated. This is especially noticed in the section on water and sewage purification, and prevention of disease especially in typhoid fever and dysentery, as well as the chapter on immunity. The work is well written, without padding, and discusses hygiene in every possible phase. It contains the best thought of the day in systematic, interesting, and instructive groupings. One criticism might be lodged against the statistics quoted in dealing with medical inspection of schools, when better and more recent ones have appeared in a publication well commented on in these same columns. With this slight criticism, the book may be well recommended to anyone interested in any of the subjects in this great field, which is now occupying so much attention in the line of preventive medicine.

F. H. K.

CEREBELLAR FUNCTIONS. By Dr. ANDRE-THOMAS, of Paris. Translated by W. CONYERS HERRING, M.D. Pp. 223; 89 illustrations. New York: Journal of Nervous and Mental Disease Publishing Co., 1912.

THIS is the twelfth volume of the monograph series issued by the editor of the *Journal of Nervous and Mental Diseases*. As heretofore stated in previous reviews, Dr. Jelliffe is to be congratulated upon his invariably good selection for his series. The present brings to the English-speaking physicians a translation

of a small book upon cerebellar functions originally in French. This work aims to bring up to date the functions of the cerebellum. Not much space is given to anatomy, but the results of experimental work are fully detailed, and then a discussion is taken up of the relation of such experimental work with actual clinical phenomena. In other words, it is an up-to-date presentation of what is known of the cerebellum, and should be in the hands of every neurologist.

T. H. W.

MINOR MALADIES. By LEONARD WILLIAMS, M.D., M.R.C.P., Physician to the French Hospital; Physician to the Metropolitan Hospital. Third edition. Pp. 396. New York: William Wood & Company, 1913.

THE author has compiled a series of lectures into a small volume, dealing with minor ailments or symptoms which are necessarily, as he says, dealt with in a cursory manner in the ordinary text-book. The minor maladies include such disorders as coughs, colds, sore throats, indigestion, constipation, giddiness, rheumatism, and similar disorders. He discusses briefly the etiology of these minor conditions and then enlarges upon their treatment. The author takes the correct view of the etiology of these ailments, laying particular stress upon the fact that while the discussed condition may be only a manifestation of a slight disorder they are frequently the expression of a serious disease which must be sought for and eliminated or alleviated before hoping to cure the minor complaint. Thus, the pretuberculous stage of phthisis, that is, the condition in which there is nothing which points to a positive diagnosis but in which there are indications sufficiently important to be greatly suspicious, is extensively considered and many persistent minor complaints or signs are shown to be directly the result of pulmonary tuberculosis. The more elaborate discussion of treatment of minor maladies is extremely valuable and thoroughly practical. Several criticisms of the subject matter may be made, however. In the first place proprietary preparations play a prominent part in much of the therapeutic advice the author gives and in the second place, medicinal treatment completely overshadows physical, dietetic, and others lines of treatment which may be employed in curing not only minor but major disorders.

In addition to the above, there are several other chapters dealing with such subjects as changes of air, general health, insanity, and a short exposition on the use of a few of the more important drugs. This last chapter is particularly timely and valuable, showing, as it does, the effects and results that can be achieved by the proper management of the old standard preparations, without the employment of the proprietaries the author recommends in the forepart of the book.

J. H. M., JR.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Oleum Chenopodii in the Treatment of Hookworm Disease.—W. SCHÜFFNER and H. VERVOORT (*Münch. med. Woch.*, 1913, lx, 129) have worked out an ingenious method for testing the efficacy of vermifuges. Their studies have been made on a very large series of cases—1457 persons infected with the hookworm and with *Ascaris lumbricoides*. The method consists in giving two treatments to a patient within a few days, the first with one drug, the second with another. This is carried out on a large number of patients. The worms recovered from the feces are counted, and the sum of the worms obtained at both treatments is determined. In this way they determine the percentage of the total number of worms originally present which were unaffected by the first drug, but which succumbed to the second. In another series of equal size, the order of the drugs is reversed. Using this method, Schüffner and Vervoort have tested the efficacy of thymol, oil of eucalyptus, beta-naphthol, and oil of chenopodium. They find the relative efficiency of the four drugs to be, for the hookworm, oil of eucalyptus, 38; naphthol, 68; thymol, 83; and oil of chenopodium, 91. For the round-worm, the same order is maintained, though the figures differ somewhat; oil of eucalyptus, 12; naphthol, 18; thymol, 78; oil of chenopodium, 87. Schüffner and Vervoort consider oleum chenopodii, which is official in the United States *Pharmacopæia*, to be a safe vermifuge, and in view of the excellent results they obtained with it, their method of administration becomes of interest. At two-hour intervals three doses of oleum chenopodii, each dose 16 drops with sugar, are given. Two hours after the last dose they give castor oil 17 grams and chloroform 3 grams.

The Examination of the Feces for Parasitic Ova.—F. WOLFF (*Berl. klin. Woch.*, 1913, 1, 301) confirms the value of Yaoita's method of examining the feces for parasitic ova. As described by Wolff, the method is as follows: From five different parts of the stool one takes a piece of fecal matter about the size of a pea; these are then placed in a test-tube with a mixture of 25 per cent. antiformin and ether in equal parts and vigorously shaken. The feces dissolve largely in this reagent with the evolution of gas. The solution is now filtered through a hair filter to remove the large food particles, the filtrate is centrifugalized one minute, and the sediment contains the ova in addition to the insoluble parts of the feces. Wolff recommends the use of the usual direct microscopic method of examination in addition to the foregoing, as it occasionally yields positive results where Yaoita's method is negative.

Study of Cultures in the Blood and Sputum in Lobar Pneumonia.—HASTINGS and BOEHM (*Jour. Exper. Med.*, 1913, xvii, 239) have studied 32 selected cases of lobar pneumonia by cultures from the sputum and blood. Positive blood cultures were obtained in 11 of these (30.3 per cent.), the pneumococcus being isolated from 9 and streptococcus hemolysans from 2. In every instance the same organism was isolated from the sputum. In 21 cases the blood cultures were negative. In 9 of these the pneumococcus was obtained from the sputum. Of the other 12, *Bacillus coli* was isolated in 2, *Micrococcus catarrhalis* in 1, *Staphylococcus* in 1, streptococcus in 2, *Bacillus influenzae* in 1. Hastings and Boehm conclude that typical cases of lobar pneumonia, in which no pneumococci are to be found either in the blood or sputum, probably exist more frequently than is generally supposed. These cases are not to be distinguished from the pneumococcus group except by blood and sputum cultures.

Pneumonic Lesions Made by Intratracheal Insufflation of Non-virulent Pneumococci.—In previously reported investigations WOLLSTEIN and MELTZER produced pneumonia in animals by the intratracheal insufflation of virulent organisms. The pneumonias produced by streptococcus and influenza bacillus were of the lobular type distinct from the lobar pneumonia produced by the virulent pneumococcus. A point recently added is the fact that in every case twenty-four hours after insufflation of a virulent pneumococcus, this organism could be cultivated from the heart's blood, whereas three or four days later, in the non-fatal cases, the lungs, as well as blood were free from the pneumococcus. This probably has its analogy in clinical findings. The conclusion was presented that different types of pneumonia are produced by specifically different bacteria. Wollstein and Meltzer (*Jour. Exper. Med.*, 1913, xvii, 353) continued the work, with the intrabronchial insufflation of a non-virulent strain of pneumococcus, to determine the influence of virulence of organisms. None of the dogs died, and few seemed ill with fever. All were killed at periods of one to seven days. The anatomical diagnosis was that of an early, not severe, lobar pneumonia in the stage of red hepatization, the condition of engorgement being still present in portions of the lobe, in the twenty-four specimens. Then followed specimens

of more advanced consolidation and, finally, in the five-day cases, resolution. The exudate left the lung framework unaffected. The lesion presented the gross appearances of a lobar pneumonia, and differed from that produced by virulent pneumococci in that the consolidation resolved more rapidly, the disease was non-fatal, the blood was not invaded, and the exudate poor in fibrin. They conclude the pneumonia caused by the streptococcus is not merely a form caused by a less virulent organism, but rather a type distinct and separate, characterized especially by the invariable leukocytic infiltration of the framework of the lungs. They later (*Jour. Exper. Med.*, 1913, xvii, 242) determined that intrabronchial insufflation of a culture of virulent pneumococcus killed by heat and still containing stainable organisms produced an inextensive, mild, patchy, superficial inflammation of the lung tissue, bearing no similarity to the lesions produced by the living pneumococcus. The insufflation of sterile bouillon caused a pronounced congestion of the lung tissue, lasting forty-eight hours.

On a Papillomatous and Carcinomatous Tumor in the Stomach of Rats Caused by a Nematode.—J. FIBIGER (*Berl. klin. Woch.*, 1913, I, 289) has made important observations on the genesis of tumors in rats, which he summarizes as follows: (1) A hitherto unknown disease of the stomach and esophagus of the rat (*Mus decumanus*) is caused by an undescribed nematode belonging to the genus *Spiroptera*. The parasite in its adult form lives in the squamous epithelium of the above mentioned organs. The intermediate host in the development of the parasite is an insect (die Schabe)—*Periplaneta americana*, *Periplaneta orientalis*. (2) The disease has been observed partly as an endemic affection in a restricted locality, partly as an experimental disease of laboratory rats induced by feeding them the infected intermediate host. (3) The initial stage of the disease consists of hyperplasia of the epithelium and inflammation. In marked cases papillomas develop; they may become enormous, filling almost the entire stomach. The papilloma may become the site of malignant degeneration of the epithelium with infiltrative growth, as happened in four of the experimentally infected animals. The malignant change occurs relatively late. (4) In two, and possibly three, of the experimentally infected rats which developed carcinoma, metastases were observed in other organs. Thus, for the first time, Fibiger says, metastasizing carcinomas have been experimentally induced. (5) In the metastases no parasites or ova were found. The development of the metastases is, therefore, to be attributed to the ability of the epithelial cells of the stomach to grow in other organs of the body without the help of a parasite. (6) So far as Fibiger's studies go, he believes it may be said that the anatomical changes found were probably due to poisonous products of the nematode. Such genesis of malignant tumors cannot be further developed with the facts thus far observed. (7) The hypothesis of Borrel and Haaland that nematodes may be a cause for the development of malignant tumors in mice and rats is confirmed by these observations. (8) Borrel's belief in the importance of nematodes for the endemic occurrence of tumors in mice is apparently correct.

Heart Size and Function in Cases of Orthostatic Albuminuria.—The diversity of opinions and findings as to the close relationship of orthostatic albuminuria to the cardiovascular system led Bass and WESSLER (*Arch. Int. Med.*, 1913, xi, 403) to study the hearts and blood pressure in 36 cases in children. The functional heart examination in each case included physical examination, orthodiography, and pulse before exercise and immediately after. In only 1 case was the heart larger than normal. Twenty-two cases show values lower than normal. Fifteen children complained of subjective cardiac symptoms or presented signs of cardiac abnormality on physical examination. All except 4 showed no enlargement by either percussion or fluoroscopy. In no case did the heart become larger after exercise. However, complaints of dyspnea on exertion, palpitation, or precordial pain were common. Twelve had distinct signs of relative heart insufficiency, as accentuated pulmonary second sound, apical systolic murmurs, booming first sounds, and increased dulness to left. These indicate dilatative weakness. The results prove that the cardiac symptoms in this distinct clinical group must find explanation elsewhere than in the altered heart size, possibly in some disturbance in the vasomotor system. The failure of the hearts to become smaller after exercise is looked upon as a restriction of the field of cardiac response. In 30 per cent. of the cases Bass and Wessler found hearts of the drop type, especially associated with other stigmas of constitutional maldevelopment.

The Treatment of Infection with Oxyuris Vermicularis.—B. HILDEBRAND (*Münch. med. Woch.*, 1913, lx, 131) has found it difficult to rid patients of infection with *Oxyuris vermicularis*. Remedies given by mouth or irrigations often fail of their purpose. He has taken advantage of the habits of the worm in attempting a cure. It is a well-known fact that the gravid female either deposits her ova in the rectum, in which case the ova pass out in the feces, or that she crawls out the anus and oviposits on the neighboring skin, usually that of the perineum. Through the itching which the crawling of the worm causes, the patient scratches the part, and thus the eggs, picked up on the fingers, may be transferred to the mouth, pass through the stomach, and develop into adult parasites in the intestine. In this manner, a constant reinfection occurs. Hildebrand finds that a salve, capable of killing the ova, ends the infection, when applied to the skin of the perineum. Morning and evening, or after defecation, the skin about the anus is thoroughly cleansed with soap and water. Then the skin is covered with a salve containing camphor, quinine, and thymol (the formula is not given). The ova which are deposited on this ointment are destroyed by it. The treatment is continued for two or three weeks. The hands and fingernails should be thoroughly cleaned after each application of the salve. The source of reinfection is thus destroyed, and in a short time the females die. Hildebrand has cured a number of cases of long duration with this method of treatment.

SURGERY

 UNDER THE CHARGE OF

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Experimental Study Concerning the Influence of an Affected Kidney upon the Kidney of the Other Side.—ISOBE (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxii, 1) says that it has long been known that a pathological condition of one kidney can exert a disturbing influence on the other kidney. This has been established in connection with wounds, tuberculosis, calculi, hydronephrosis, and tumors. They may lead to a marked diminution of the urine, even to anuria. A nephrectomy or nephrotomy of the affected kidney may cause an increase of the urine. From his experimental studies, Isobe believes that when the lesion of one kidney is severe the products of decomposition are absorbed into the blood and produce a toxic effect upon the epithelium of the other kidney and more or less severe parenchymatous changes in it. When wounds of one kidney are of very mild grade, so that only little toxic substance is produced, there develops only a more or less distinct hypertrophy of the other kidney. The decomposed kidney substance is, according to Isobe's view, specifically toxic and acts upon the kidney alone. From a practical standpoint, a diseased kidney on one side calls for operation as early as possible, before the degenerative changes in the other kidney can occur.

Fat Embolism of the Systemic Circulation and its Cause.—FROMBERG (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxii, 23), from a clinical, autopsy, and histological study of one case and a study of the literature, says that fat emboli in the systemic circulation are rare. Multiple miliary hemorrhages, seen at autopsy after an accident, should always arouse suspicion of fat emboli. The number of small hemorrhages in the brain is probably an indication of the severity of the condition of fat embolism. Emphasis is to be laid on the fact that hemorrhages in the cortex are rare. Fat embolism in the systemic circulation favors the deposit of masses of fat in the lung, which filters the fat out of the blood, favors increase of the lumen of the lung capillaries, and increased pressure in the lung vessels. Fromberg believes that he has shown that the persistence of the foramen ovale is an important factor in the production of fat embolism in the systemic circulation. In future cases attention should be directed to

the foramen ovale to determine whether and how often fat embolism can develop in the systemic circulation in the presence of a closed foramen ovale.

A Contribution to the Question of the Origin of the So-called White Bile with a Complete and Permanent Closure of the Common Bile Duct.—BERTOG (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxii, 49) says that hydrops of the whole biliary system is not a rare occurrence. He believes that the closure of the common duct must be absolute and permanent to produce this result. This will be due in most cases to a tumor, but it may be due to closure by a calculus, if the complete closure lasts long enough. The time from the occurrence of the closure to the appearance of the so-called white bile, is variable. It must be long enough, however, for the absorption of all the bile in the biliary passages. The pressure in the ducts must be high enough to overcome the pressure of the secretion in the liver. There need not be present a hypersecretion of mucus in the bile ducts, but the dilated ducts will be filled with mucus to such an extent that the bile produced in the liver cannot get into the ducts. The secretion of the bile by the liver cells gradually decreases in consequence of the stasis in the biliary passages.

The End-results of Radical Operation for Knee-joint Tuberculosis in Adults.—MAY (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxii, 171) says that his work is a continuation of the investigations of Brandes concerning the end-results of radical operation for knee-joint tuberculosis in children, and was done to determine whether the curved resection method of Helferich gives better results than other methods. Helferich's method as applied to adults is briefly outlined as follows: Under narcosis and with a bloodless limb, two lateral skin incisions are made and united by an anterior transverse incision. After turning up the skin flaps, the capsule and patella are extirpated. Then with a Helferich saw, an arched, thin layer of cartilage and bone are removed from each joint end. The wound surfaces are then covered with an iodoform mixture, and the bone ends adapted to each other. Usually the only fixation of the bone ends consisted of cat-gut sutures passed through the edges of the bones and the ends of the sutures brought out of the two lower ends of the longitudinal skin incision to act as drains. An exact extension position is maintained between the resected surfaces, as a rule, by a splint and bandage, which is removed for the first time in about three weeks. The sutures are then removed and, if the extension position is not complete, it is corrected under narcosis and a plaster cast is applied. The patient is then discharged from the hospital, but wears the cast eight months longer, and after that a leather support. Within the nine years from 1898 to 1907, 76 radical operations were performed on adults in Anscutz's clinic in Kiel, for tuberculosis of the knee-joint. The operations performed were as follows: 3 arthrectomies, 8 primary amputations, 57 resections, and 8 secondary amputations. Almost all those still living have been personally examined. None shows any noteworthy flexion. In only one was there marked shortening which, however, existed before the resection. The Helferich excision produces an average shortening

of 3.7 cm. 76.4 per cent. of the adult cases have, from resection, the prospect of a useful limb. Three-fourths, or 77.8 per cent. of the fatal cases were due to the tuberculosis. All of the 32 living patients possess, today, a firm ankylosis and are capable of earning their living with the exception of 2. The cause in these is tuberculosis elsewhere. Of those aged over forty-five years, success was obtained in 50 per cent. Resection may be advised at this age in suitable cases.

Radical Operation for Intestinal Herniæ with Incomplete Hernial Sac (Gliding Herniæ).—SCHMIDT (*Deutsch. Zeitschr. f. Chir.*, 1913, cxxii, 266) says that in gliding herniæ on the right side, the involved portion of the intestine has a single limb, on the left side it is in a loop with two limbs, an afferent and efferent. To find the empty portion of the hernial sac, an effort should be made to pick up a fold of it between the fingers and prove the mobility of the layers on each other. The reposition of a portion of the sac, whether it has been opened or closed by sutures after being opened, is produced by inversion. The excess of sac should be excised before reposition, but that portion containing the vessels nourishing the intestine, must be spared. To recognize this portion, the sac should be so held as to transmit light through it. Generally, there is no danger in cutting away the anterior layer of the sac from the internal angle of the hernial orifice around the orifice to the junction of the serosa of the sac and intestine, and then along this junction throughout. A flap of hernial sac may be preserved from this portion. In isolated gliding hernia of the appendix, the latter and the sac should be removed. If the ileum is involved in the hernia, the sac below the hernia should be removed. On the left side the loop formation calls for later flaps from the convex margin of the intestine. Not rarely the separation of the hernial sac from the spermatic cord proves very difficult, and castration is repeatedly necessary. In such cases it will be better to implant the testicle and cord in the abdominal cavity.

The Reduction of Fractures by Local Anesthesia.—DOLLINGER (*Zentralbl. f. Chir.*, 1913, xl, 763) reduces simple fractures of the extremities under the control of the fluoroscope or skiagraph and fixes them immediately by a plaster cast. Recently he has added the use of local anesthesia. The anesthetic employed was novokain-suprarenalin solution, and was injected either between the fragments or around the limb above the fracture. In using the first method he established the site of fracture by the x-rays, and then injected 10 to 20 c.c. of a 1 per cent. novocain-suprarenalin solution exactly between the fragments. Unless this is accomplished, complete success will not be attained. Anesthesia is obtained within five to ten minutes, after which the fragments can be manipulated without pain. This method has the following disadvantages: (1) The usual acute tenderness at the seat of fracture makes the introduction of the needle very unpleasant. (2) The blood clot between and around the fragments may prevent the anesthetic fluid from coming into direct contact with the nerves, while it may find its way into the open vessels and cause toxic symptoms. (3) The exact location of the fracture may be

very difficult in fat people or in the presence of hematoma formation, so that the placing of the fluid between the fragments, may be difficult. These disadvantages probably explain why this method has not received general support. The circular injection method gives much better results. After disinfection of the skin with tincture of iodine, the whole circumference of the limb is injected about four fingers' breadth above the fracture. If there is a large hematoma, the injection may be made higher, even 10 to 20 cm. above the fracture and above the hematoma. First the skin and subcutaneous tissue are infiltrated, and then the deeper layers until the whole thickness of the limb is infiltrated. As few punctures as possible should be made. For the leg three or four are sufficient, for the thigh four or five, and for the forearm two. In about ten minutes after the infiltration there will be complete anesthesia peripheralward, and the reflex muscle spasm will be overcome. The fracture can then be manipulated without pain. One patient with a Pott's fracture, after infiltration, stood on that limb without pain, although the limb bent at the fracture. The ease with which the reduction can be accomplished without muscle spasm is striking. Dollinger would restrict the use of the first method, or injection between the fragments, to those cases in which the circular method of anesthesia is impracticable because of the anatomical situation of the fracture, as in fracture of the clavicle, pelvis, vertebrae, and ribs.

Perirenal Hematoma.—SPEESE (*Surg., Gynec., and Obstet.*, 1913, xvi, 571) says that perirenal hemorrhage is caused by tuberculosis, abscess or tumors of the kidney, necrosis of the adrenal gland, traumatism, and occasionally arises in hemophilia. The spontaneous form is probably due to chronic nephritis, the only pathological lesion which has been demonstrated. The characteristic symptoms of the disease are sudden pain, the signs of internal hemorrhage, and the formation of a retroperitoneal tumor. A moderate degree of hematuria is present in one-third of the cases. Functional tests show diminution in the secretory activity of the kidney. The affection is most commonly mistaken for intestinal obstruction or paranephritic abscess. The disease pursues a rapid course if unrelieved, death resulting from hemorrhage, infection, or pulmonary complications. Medical treatment has been uniformly unsuccessful. Ten of the cases operated on have recovered (62 per cent.). The mortality of the 21 cases treated by both surgical and medical measures is 52.5 per cent.

Arthroplasty.—MURPHY (*Annals of Surgery*, 1913, lvii, 593) says of orthroplasty, which he discusses in an extensive paper, that perfectly movable, normally functioning joints with sliding and rotary motion of the normal type, can be and have been reproduced. A new synovialized membrane is produced with fluid not synovial, but resembling synovial fluid, and lining cells identical with those lining hygroma, and closely resembling the endothelial cells of normal synovial membrane. These joints support full weight and traction. They are painless once the process of repair is complete. They are not subject to the hematogenous metastatic arthritides of normal

joints. A fibrocartilage-like structure develops on the end of the bone, and the latitude of motion increases with time up to the full anatomic limitations in the uncomplicated cases. The production of new joints is not difficult technically, nor is it associated with great danger to life.

THERAPEUTICS

UNDER THE CHARGE OF

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Vaccine Therapy of Carcinoma.—LEWIN (*Therapie d. Gegenwart*, 1913, liv, 253) reports a case of carcinoma of the breast where the subcutaneous injections of the patient's own ascitic fluid had a remarkably good effect upon the patient's condition, so that she was apparently cured, and was in comparatively good health eighteen months after her discharge. This patient had first one breast and then the other amputated for recurring carcinoma and subsequently developed ascites that required repeated tapping. Each time 10 c.c. of the fluid was reinjected subcutaneously before the needle was withdrawn. It seemed that she would have less than a month to live, when first seen, and the marked benefit seemed to be due to the injections. He also reports a second patient who, after removal of one breast for carcinoma, had a recurrence in the other breast. She was given five injections of an autolysate of cancer cells. The recurring nodules gradually disappeared, and the patient, observed now for one year, has been apparently cured. Lewin does not suggest this method as a cure nor indeed as a substitute for surgery, but thinks it may be of great service in inoperable cases, and as an aid to x-ray treatment or other measures.

Chronic Arthritis; Therapeutic Evidence of the Incidence of Streptococcal Infection.—JONES (*British Med. Jour.*, 1913, 2733, 1047) says that this paper is a contribution to the bacteriological diagnosis of arthritis based on the results of empirical therapeutic measures. It contains the results of 20 cases suffering from arthritis of various types, in all of which a tentative clinical diagnosis of streptococcal infection was made and which were treated with vaccines of streptococci derived from different sources. They do not go to show that all cases of arthritis are due to streptococcal infection, for the tubercle bacillus, gonococcus, and pneumococcus are all well known to infect joints. If, however, therapeutic results can be accepted as a basis of bacteriological diagnosis, at least eight of these indicate that streptococcal infection is concerned in cases of chronic arthritis. The cases were, in the majority of instances, of long standing, they had resisted general therapeutic measures, and no source of infection

was clearly indicated. Effusion into the joints was rare, and the fluid when removed by puncture was invariably sterile. Blood cultures were also sterile whenever investigated. For various reasons streptococcal infections were suspected and the patients were accordingly treated with vaccines made from streptococci obtained either from the mouth, in cases of oral sepsis, from the urine, or from the feces. Of the 20 cases treated, 1 case was completely cured, 6 were markedly improved; 6 only slightly benefited; 6 not effected, and 1 was made distinctly worse. Jones believes that his therapeutic results justify the conclusion that arthritis may be caused by streptococcal infection chiefly derived from some part of the gastro-intestinal tract.

Benzol in Leukemia.—RÖSLER (*Wien. klin. Woch.*, 1913, xxvi, 838) reports 2 cases of leukemia, 1 with a leukocyte count of approximately 200,000, and the other with 237,000 leukocytes, successfully treated with benzol. The benzol treatment seemed to cause at first an increase in the leukocytes to nearly 340,000 and 420,000 respectively in the 2 cases. After this preliminary increase in the number of the leukocytes the blood picture began to improve as well as the general condition of the patients. The patients consider themselves cured but the period of observation has been too short to admit of any definite conclusion. The only untoward symptoms observed during the benzol medication were digestive disturbances consisting of oppressive and burning sensations in the stomach and a temporary loss of appetite.

Syphilitic Pernicious Anemia.—WEICKSEL (*Münch. med. Woch.*, 1913, lx, 1143) reports a case of advanced pernicious anemia in a patient having a positive Wassermann reaction. He found in the literature reports of a number of cases of syphilis with an anemia closely resembling pernicious anemia which improved under antisiphilitic treatment. The patient observed by Weicksel was treated by salvarsan and three months after the first injection the Wassermann reaction became negative. The patient's blood and general condition improved steadily. He believes that this result suggests that salvarsan may be beneficial in the treatment of pernicious anemia. Bramwell has reported a number of cases of pernicious anemia treated with salvarsan with great benefit, and attributes the beneficial effects to the arsenical composition of salvarsan.

The Treatment of Amebic Dysentery by Emetin.—BAERMANN and HEINEMANN (*Münch. med. Woch.*, 1913, lx, 1132, 1210) have used emetin in the treatment of 22 cases of amebic dysentery. They consider it a most efficient remedy, although only 6 of the 22 cases were cured. The best results were obtained by injecting intravenously 150 to 200 milligrams in 100 c.c. of salt solution, repeating the injection after eight or ten days. It is also necessary to supplement the intravenous injections by four or five subcutaneous injections of 100 to 150 milligrams at two- or three-day intervals. This after treatment should be repeated at intervals of three or four weeks. Baermann and Heinemann believe that this treatment is more successful in the early cases. A great number of cases relapse and the examination of the stools for amebæ should be kept up for months. This treatment is

based upon rational therapeutics as it has been found that ipecac has a specific action against amebæ. However, ipecac cannot be given in sufficiently large doses on account of untoward by-effects. Emetin is an alkaloid derived from ipecac which Rogers has used with brilliant success in the treatment of amebic dysentery. A dose of emetin containing seventy times the usual dose of ipecac can be given without any untoward by-effects. Baermann and Heinemann state that the maximum intravenous dose of emetin is 250 mg. per 60 kg. of body weight.

Results of Serum Treatment in 1300 Cases of Epidemic Meningitis.—FLEXNER (*Jour. Exp. Med.*, 1913, xvii, 553) gives a final summary of nearly 1300 cases of epidemic meningitis treated by the serum prepared by the Rockefeller Institute. The antimeningitis serum was first employed in 1906, and the latest figures relating to its use included in this report were furnished in 1912. He says that there is no longer doubt that the serum has come to be applied under conditions fairly representing all known manifestations of epidemic meningitis. Hence the test of the serum treatment may be regarded as having been a rigorous one. The mortality of all cases was 30 per cent. The average mortality of the disease not treated by serum is at least 70 per cent. Furthermore, complications and sequellæ are reduced in number. In fact, the number of permanently injured among the serum treated has become very small. Of all the severe sequels, deafness has remained least influenced. Unhappily, injury to the internal ear takes place very early and sometimes before the diagnosis of meningitis has been made. In view of the great reduction in other severe effects, Flexner hopes that even this one may be diminished by a more uniformly early application of the serum. The arthropathies have not only been reduced in frequency, but they have been shown to be amenable to direct injections of the serum. Undoubtedly the tendency to hydrocephalus in the young has been diminished, and the intraventricular injection of the serum has operated in several instances to abolish infection and inflammation of the cerebral ventricles, and to reestablish communication between the ventricles and the subdural space of the spinal cord.

The Prophylaxis and Treatment of Diphtheria.—SCHREIBER (*Deutsch. med. Woch.*, 1913, xxxix, 928) states that his results show that the active immunization suggested by von Behring is entirely harmless and effective as a method of producing protection against diphtheria. He says that the preparation develops an immunity against diphtheria that persists for a much longer period of time than the present method of injecting prophylactic doses of diphtheria antitoxin.

Old and New Salvarsan.—GUTMAN (*Berl. klin. Woch.*, 1913, I, 581), in comparing salvarsan with neosalvarsan, says that the percentage of febrile reactions is somewhat higher after salvarsan than after neosalvarsan, notwithstanding correspondingly larger doses of neosalvarsan were used. Gutman thinks it is probably due to individual susceptibility to salvarsan or to the injection of a hypotonic solution. Gastro-intestinal disturbances were much more marked with salvarsan,

and reactions similar to anaphylaxis occurred after a considerable number of salvarsan injections but not after neosalvarsan injections. No difference or very little in therapeutic effect could be determined.

The Therapeutic Value of Diuretin in Acute Experimental Nephritis.—CHRISTIAN AND O'HARE (*Arch. of Int. Med.*, 1913, xi, 517), in their conclusions, state that diuretin given to rabbits with a severe, fatal, experimental nephritis shortens the duration of life of these animals. On the other hand, 9 out of 12 rabbits which survived the experiment had received diuretin. This work supports the view that in a severe acute nephritis a diuretic drug, such as diuretin is contraindicated, inasmuch as in the experiments diuretin shortened the lives of the animals. On the other hand, of the survivors a large proportion, three-fourths, had received diuretin. This rather gives support to the view that in less severe cases diuretin may be beneficial, and so justifies the cautious use of the drug in moderately severe cases of acute nephritis. In the survivors it is not certain that acute severe renal lesions were produced. Consequently deductions from these relatively few survivors are of less value than from the larger number dying during the experiment. Of course, it is realized in making deductions such as the above, that they may not be applicable directly to conditions in the human being, for due allowance must be made for the many differences between man and the lower animals. The experiments, however, certainly support the view that diuretin as a diuretic drug may be harmful in a case of acute nephritis.

The Treatment of Malignant Pemphigus by Intravenous Injection of Human Blood.—PRAETORIUS (*Münch. med. Woch.*, 1913, lx, 867) reports that a woman, suffering for two years from a severe pemphigus which had resisted all therapeutic measures, was completely cured by one intravenous injection of 20 c.c. of fresh human blood. The blood was obtained from the donor by syringe, and immediately injected into the patient's vein. No by-effects were observed, and by the third day distinct improvement was noted, and at the end of a week the recovery was complete. The cure has now lasted for a period of eight months, with absolutely no sign of recurrence. Praetorius believes that there is no danger in the use of non-defibrinated blood if the blood is obtained rapidly and fairly fine needles are used, so that the passage of large coagulæ are prevented.

OBSTETRICS

UNDER THE CHARGE OF

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Pregnancy Complicated by Abnormal Conditions in the Pelvic Viscera.—WALLART (*Monats. f. Geburt. u. Gynäk.*, 1912, xxxvi, No. 5) has studied the changes produced in the Fallopian tubes by

pregnancy, and illustrates his article by microscopic pictures. He believes that the changes in the tubes are practically those which go on throughout the uterus. As the fundus rises, the tubes become longer and considerably stretched. Those who have studied the subject believe that the increase in size in the tube during pregnancy may be referred to the growth of the unstriped muscle fiber. If a tube be cut in a cross-section, the dilatation and engorgement of the vessels attract attention upon microscopic examination. During operations upon the tube in pregnancy, one often sees apoplexies in the connective tissue of the tube, which confirms the microscopic appearance. The connective tissue and fibrous tissue is enlarged, and the cellular elements are increased. Leukocytes are abundant as well in the vessels as in the connective tissue. Their number may be so great as to resemble abscess formation. In examining a Fallopian tube removed during the last month of pregnancy, the abundance of round-cells was very noticeable, and the nuclei stained dark, with little protoplasm. Among them were many long, clear nuclei, with abundant processes. Masses of protoplasm were found with varying nuclei, and abundant migratory cells. Syncytial changes seem to have occurred in the endothelium. The formation of decidua was plainly demonstrated, not only by the presence of decidual cells, but by the formation and arrangement of the cells. Villi were present, and syncytial cells also. In ectopic gestation there seems to be little difference in the decidual reaction and formation in the tube. In the uterus in ectopic pregnancy, the uterine decidua seems much more abundant than that in the tube.

ANDREWS (*Jour. Obstet. and Gyn. of British Empire*, October, 1912) reports the case of a multipara who, on rising from the floor, had a sharp pain in the right side of the abdomen. There was no vomiting, and the pain was made worse by the motions of the child. The pulse and temperature were normal, there was a tense spot just above and internal to the right anterior spine, without rigidity. There was no evidence of involvement of the right kidney, and vaginal examination was negative. A diagnosis at the time was impossible, and the patient was ordered to remain in bed, to have the bowels moved, and to use counter-irritation. Three days afterward the abdomen became greatly distended, the pain was severe, peristalsis was visible, and the patient was vomiting. Upon section, a small, purple body was seen in the right iliac fossa attached to the fimbriated extremity of the right Fallopian tube. It seemed to be a soft structure which had become solid as the result of thrombosis. The tube, ovary, and appendix, were normal. The small purple body was removed after ligating its attachment to the fimbriated extremity of the tube. There was no abnormality about the abdominal contents, but the abdominal wall was very thin. The patient suffered greatly after operation from distention of gas, but gradually recovered. Microscopic examination showed the tumor to be a thin-walled cyst filled with blood-clot. It was apparently a twisted hydatid of Morgagni, which must have been about the size of a small grape before torsion occurred.

GRADL (*Zentralbl. f. Gynäk.*, 1912, No. 17) reports the case of a multipara with double gonorrheal pyosalpinx. The uterus was edematous and somewhat swollen. The tumors were so adherent that it

was thought unwise to remove them, and it was hoped that spontaneous evacuation of pus through the rectum would occur. This subsequently happened, the tumors disappeared by vaginal examination, and the patient was discharged from the hospital. She afterward returned pregnant, complaining of pain in the abdomen and an abundant discharge of pus through the rectum. The pain became so great that the patient demanded that abortion be produced. This was declined, and the patient went to term, giving spontaneous birth, in normal labor, to a living, normal child. The child had no ophthalmia and seemed vigorous. The case is interesting because of the double pyosalpinx, and the discharge of pus through the rectum for more than half of the pregnancy. In spite of this, mother and child escaped infection during labor and in the puerperal period.

FRIES (*Zentralbl. f. Gynäk.*, 1912, No. 37) reports the case of a primipara about four months pregnant, who suffered from frequent vomiting and severe pain in the right side of the abdomen. Examination revealed a tumor which seemed to be an ovarian growth. At operation, the tumor was found in the right broad ligament, extending to the fundus. This proved to be an echinococcus cyst complicated by the presence of an intraligamentary myoma on each side. The patient recovered without the interruption of pregnancy. Labor came on at term and was long and tedious, but was finally terminated with delivery by forceps. The child was unusually large and was born asphyxiated, but recovered. Mother and child made a good recovery.

Chorionic Villi in the Uterine Wall Eighteen Years after the Last Pregnancy.—RIES (*Amer. Jour. Obstet.*, March, 1913) reports a very suggestive case which has to do with the question of development of chorio-epithelioma malignum. His patient was a negress who sought hospital treatment for uterine hemorrhage. Her history stated that menstruation had always been profuse, she had married at eighteen years, and had four full-term labors with normal pregnancies and natural delivery. There was no excessive hemorrhage or infection, and she had nursed each child about four months. She had had four abortions from unknown causes. There had been no complications with these abortions. Recently, menstruation had been prolonged and unusually frequent, causing profound anemia. Upon examination, she had a mass of fibroids in the uterus. At operation, the body of the uterus with the fibroid mass and the appendix were removed. The patient's recovery was uninterrupted and complete. Upon examining the specimen, the uterine cavity was smooth and lined with a thin mucous membrane. A peculiar white, translucent, thread-like formation protruded from the cut surface of the uterus where it had been separated from the cervix. Upon dissection, it was found to be contained in a large vein. By splitting up the vein and following upward, this thread-like mass reached the left uterine cornu, where it was attached to the wall of the vein. The thickness of the uterine wall was about 3 cm. The thread-like mass was solid, and its lower end slightly clubbed. Upon cross-section through the uterine cornu, one vein was filled with these whitish formations resembling grapes, and this mass could be withdrawn from the vein. Others showed a similar appearance. Upon examining the tissue microscopically,

these masses were found to consist of chorionic villi which had undergone fibrinous and hyaline degeneration. At several points the villi invaded the substance of the uterus. This case explains some late appearances of chorio-epithelioma malignum at long and irregular intervals, after a partial or complete abortion.

The Difficulty of Producing Sterility by Operations on the Fallopian Tubes.—LEONARD (*Amer. Jour. Obstet.*, March, 1913) reports from the Johns Hopkins clinic two cases where the attempt had been made to produce sterility by ligating the Fallopian tubes with silk. In both cases the attempt was unsuccessful, the patient afterward conceiving. Reference to the literature shows that section and resection of the tubes between two ligatures is also unreliable, and that resection of the tubes between two ligatures with burial of the uterine end may be followed by conception. The cautery is no more successful, and even bilateral salpingectomy has failed. The attempt has been made to produce sterility by resecting interstitial portions of the tube by the removal of a wedge-shaped piece from the uterine cornu. While this is in many cases successful, it has not been so in all. Experiments upon animals have led to no definite conclusion, except that it is probably necessary to insure sterility by removing the entire Fallopian tube, together with the interstitial portion of the uterine cornu.

The Effect upon Pregnancy and Labor of Ventro-enucleation of Intramural Fibroids.—ENGSTROM (*Monats. f. Geburts. u. Gynäk.*, 1912, xxxvi, Festnummer) has studied the results of ventro-enucleation of intramural fibroids in 27 patients in whom conception afterward occurred. The size of these tumors had varied from 5 as large as a child's head to those as large as an egg. In 3 cases, the tumors were in groups in different portions of the uterus. One patient conceived soon after operation, 7 within six months, 5 within a year, 9 between one and two years, 3 between two and three years, and 3 after three years. In 20, pregnancy proceeded normally; 12 patients had borne each one child, and 1 patient six children; in 20 of them 1 patient had abortion; 2 premature birth; in 1 case the fetal heart sounds ceased four weeks before birth; and in 2 cases there was twin pregnancy, the children dying soon after labor. In all, there were 7 cases in which the one pregnancy, which occurred after operation, terminated in abortion. So far as could be traced, this result could not be ascribed to operation, and these patients were treated outside the clinic by physicians unknown to the hospital. The most probable reason for the abortions was thought to be some chronic inflammation of the endometrium. Among these 27 patients were born 38 fully developed children, and, in 3, premature children, without apparent injury to the uterus. There was but 1 artificial labor terminated by the high application of forceps. In but 1 case was the puerperal period complicated, and that by prolonged hemorrhage.

Ectopic Pregnancy.—LUCY (*Jour. of Obstet. and Gyn. of British Empire*, March, 1912) reports a case of combined pregnancy in which the patient, after severe abdominal pain, collapsed, and later expelled from the uterus a four-months' fetus without the placenta. This was followed by abdominal distention and fever, great pain and shock,

and swelling of the right iliac fossa. Upon section, the right tube had ruptured and had contained a four-months' fetus which was lying among the intestine. Upon opening the uterus, the placenta and the first fetus was found firmly attached. The corpus luteum of the right ovary was of more recent date than those of the left.

A case of ovarian pregnancy, illustrated by a very clear drawing, is reported by BANKS (*Jour. Obstet. and Gyn. of British Empire*, April, 1912). The case was typical of ectopic gestation, and this diagnosis was made upon examination. At section, a tumor upon the right side consisted entirely of ovary, the normal tube being free. A small portion of ovarian tissue was left, and the cut edges closed with catgut. The patient made an uninterrupted recovery. Upon microscopic examination, the pregnancy was clearly ovarian, and the growth of the villi had been similar to that observed in tubal gestation.

Primary abdominal pregnancy is reported by RICHTER (*Archiv f. Gynäk.*, 1912, xcvi, No. 3). The patient was admitted to hospital following severe pain in the lower abdomen, with collapse. Upon examination there was dulness above the symphysis, and abdominal tenderness. Upon vaginal examination, the uterus was small, ante-flexed, and there was no tumor of the Fallopian tube. An indefinitely outlined mass could be made out behind the uterus. A diagnosis of probable tubal abortion was made, and operation was performed. Upon section, intra-abdominal bleeding was present, which could not be traced to the tube or ovary. The ovum was found implanted upon the rectum, both Fallopian tubes being normal. The ovum was removed and the tissues closed by suture. On examination, the villi of the chorion had penetrated the wall of the intestine for a considerable extent, and there was every evidence that pregnancy had been primary and abdominal. The patient's recovery was uninterrupted.

JELLINGHAUS (*Amer. Jour. Obstet.*, April, 1912) describes an interesting case of true ligamentous unruptured tubal pregnancy of eight months. The patient had been treated in the hospital for pelvic exudate without relief. When seen, the tumor was the size of an eight-months' intra-uterine pregnancy, and there was no sign of fetal life. Examination under anesthesia showed that an unruptured tubal pregnancy of about eight months was present. The fruit sac, with the placenta and membranes, were removed by section. The patient's recovery was complicated by vaginal and abdominal fistulae and urinary fistula, probably caused by pressure of gauze packing. This gradually closed.

Interstitial pregnancy is reported by MARKOE (*Amer. Jour. Obstet.*, April, 1912) in a patient who, five years previously, had been admitted to hospital with what was believed to be incomplete abortion. Curetting failed to discover the fetus. The patient left the hospital against the advice of the physician, but returned in collapse with rapid pulse and high fever. After several months she was sufficiently recovered to leave the hospital. When she returned five years later she stated that she had been delivered three years previously, with instruments, of a large stillborn child. Vaginal examination showed a tumor on the right side of the uterus, very tender, and slightly movable. Upon section, the tumor was directly connected with the right cornu of the uterus. Upon examining the specimen, interstitial pregnancy was found to be present.

GYNECOLOGY

UNDER THE CHARGE OF

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Dangers of the Trendelenburg Posture.—The opinion that more fatalities during anesthesia result from an increased flow of blood to the heart than from the opposite condition, a diminished supply resulting from hemorrhage or so-called surgical shock, is expressed by GATCH and his associates (*Jour. Amer. Med. Assoc.*, 1913, lx, 1273). From both clinical observations and animal experiments, they have come to the conclusion that a very severe, and at times fatal, strain can thus be thrown on the right heart when a condition of asphyxia exists in conjunction with the Trendelenburg position. The entire vasomotor mechanism, wherewith the body normally compensates for the effects of gravity on the circulation, being deranged under these circumstances, the blood pressure is raised, and at the same time the head-down posture causes every drop of blood passing through the capillaries of the abdomen and legs to return quickly to the heart—a condition which is not present when asphyxia occurs with the body in the horizontal or upright position. This return of blood to the heart may be so excessive as to subject that organ to an undue strain, and if the patient struggles, or pressure is made on the intestines—as by extensive packing-off—the state of affairs is rendered much worse. In the absence of asphyxia, however, it is doubtful if these agencies can injure a normal heart. The authors believe, as a result of their studies, that patients with well-marked cardiac disease either should not be placed in the Trendelenburg posture at all, or that this should be used with the most extreme caution, the horizontal position of the body being changed to the head-down one very gradually, so as to prevent a too sudden inflow of blood to the heart, and in all cases, they consider it of great importance to conduct the entire anesthesia without permitting the patient to become cyanotic at any time, making use of a preliminary injection of morphine if necessary to secure this result.

Effect of X-ray Treatment of the Ovaries upon Exophthalmic Goitre.

—An interesting clinical contribution to the much-discussed question of the relationship between the thyroid and the female genital glands is furnished by the report of MAMMABERG (*Wien. klin. Woch.*, 1913, xxvi, 693) who has subjected 10 women suffering with the classical symptoms of Basedow's disease to Röntgenization of the ovaries. They were all treated as ambulatory patients, their manner of living being in no wise altered, so that the results observed must be considered due to the treatment itself, and not to any extraneous factors, such as rest, improved care, or diet. The number of exposures given varied from 3 to 15. In 8 of the 10 patients a marked increase in

body-weight occurred, amounting in one instance to 21 per cent. of the patient's previous weight, and averaging about 11 per cent. of this. In half the cases the exophthalmos was unaffected, but in the other half it was distinctly reduced, in one instance disappearing completely. Practically no effect was produced upon the size of the goitre, some of the patients showing a slight increase in this, others a slight decrease. The most marked improvement noted, however, was in the subjective condition of the patients; with only one exception (a woman treated but a very short time) all the distressing symptoms of the disease disappeared, the patients felt entirely well, and were able to return to their regular work, which in several instances they had been forced to abandon. A troublesome diarrhea which was present in several disappeared after a few treatments. Mammaberg says that he has now been experimenting with this form of treatment for about a year and a half, and although as yet he cannot speak of any case as being completely and permanently cured, he thinks the results so far attained justify more extensive investigations along this line. He considers the apparent benefits which follow the treatment to be due to some quantitative or qualitative alteration produced by the x-rays upon the internal secretion of the ovaries, this probably consisting in the suppression or reduction of some substance formed in them which has an action upon the thyroid, stimulating it to the production of substances which cause the symptom complex of Basedow's disease. Direct radiation of the thyroid itself, on the other hand, is apparently without effect, two patients in whom this was tried following the ovarian treatment showing a distinct retrogression, and a third remaining entirely unaffected.

Thyreogenic Origin of Uterine Hemorrhage.—Another paper dealing with the relations of the thyroid to the female generative system has recently been published by SEHRT (*Münch. med. Woch.*, 1913, lx, 962). He reports that in 13 out of 20 patients suffering from uncomplicated "metropathic" hemorrhages, without demonstrable anatomic basis, all the distinctive blood-changes were found which have been described by Kocher as characteristic of hypofunction of the thyroid gland—a relative neutrophilic leukopenia, with corresponding lymphocytosis, a total leukocyte count below 6000, and a marked reduction in the coagulation-time of the blood. In 6 of the remaining 7 cases the coagulation-time was decreased, but either the neutrophilic leukopenia or the lymphocytosis was lacking. Sehrt expresses the belief that disturbances of the normal relations between the thyroid and the ovaries may perhaps be the cause of these hemorrhages, which have as yet remained unexplained on anatomic grounds, many cases of so-called "metropathia hemorrhagica" representing, in fact, abortive cases of myxedema, and, further, that insufficient activity on the part of the thyroid gland may have some causal relation to the production of eclampsia.

Diagnosis of Renal Tuberculosis.—In discussing the very important question of the determination of the presence or absence of tuberculosis in an apparently healthy kidney in the presence of known infection of the other, CASPAR (*Deutsch. med. Woch.*, 1913, xxxix, 1140) says

that he believed that any urine, no matter how nearly normal chemically and microscopically, which caused tuberculosis in injected guinea-pigs, indicated a positive tuberculous infection of the kidney from which it was obtained. Later researches by himself and others have shown, however, that this is not always the case. He has found that while an entirely *healthy* kidney never secretes urine containing tubercle bacilli, a *nephritic* organ (not tuberculous) may transmit and excrete tubercle bacilli which are circulating in the blood, without itself containing any tuberculous focus. If the urine, obtained by ureteral catheterization, contains at several examinations albumin and tubercle bacilli—perhaps, though not necessarily, casts also—it is safe, in Caspar's opinion, to assume that the kidney itself is not tuberculous. If, however, leukocytes and red blood cells are present in addition, the question becomes more complicated, as these may indicate the presence of a destructive tuberculous process in the kidney. They may also be present, however, merely as a result of the nephritis, without any such destructive process. In such cases, Caspar bases his differential diagnosis on the fact that in a moderate degree of toxic nephritis—which alone could come into consideration—leukocytes and red blood cells are present in the urine only in very limited quantities, and as a rule not constantly; albumin and casts are present, moreover, in amounts greater than can be accounted for by the corpuscular content, while the kidney function as estimated by the various functional tests—is well preserved. In the case of true renal tuberculosis, however, the urine is much richer in leukocytes and red blood cells; casts are very scanty, or entirely absent, and the functional activity is markedly reduced.

Histology of the Corpus Luteum.—A few points of interest are brought out in a recent paper by MILLER (*Berl. klin. Woch.*, 1913, i, 865) with regard to the histogenesis of the corpus luteum, and the differential diagnosis between the corpus luteum of menstruation and that of true pregnancy. Miller says that he has found in the cells of numerous corpora lutea of pregnancy small droplets of colloid material, a substance which, in his opinion, can arise only as a result of degeneration of *epithelial* tissue, this finding furnishing, therefore, further evidence in favor of the now pretty generally, though not universally, accepted theory of the epithelial origin of the corpus luteum, as opposed to that of its stromatogenic origin. Miller has never found this colloid material in corpora lutea menstruationis; these undergo a fatty degeneration, small droplets of neutral fat, demonstrable by Sudan III, appearing as soon as retrogression begins. Moreover, small foci of calcification are quite common in corpora lutea of pregnancy, but are very rarely found in those of menstruation, and are therefore also of value from a diagnostic standpoint. That this question is not a purely academic one is illustrated by a case which Miller quotes. A patient, aged fifty years, in whom the possibility of pregnancy had not been thought of, was operated upon for cystocele by the Schauta-Wertheim method (interposition of the uterus between the vagina and bladder), at the same time, one tube and ovary being removed for some reason, and sent to the laboratory. Upon receiving the pathologist's report that the latter organ contained

a large, fresh corpus luteum, the surgeon remembered that the uterus at operation had appeared rather large, soft, and hyperemic, and was greatly worried lest he had performed the interposition operation upon a pregnant uterus, a procedure which would surely lead to serious results unless early abortion should occur. A more careful examination of the corpus luteum, however, demonstrated the presence of numerous fat droplets, without colloid or calcification, upon which the definite diagnosis of a corpus luteum menstruationis was made, a diagnosis which the subsequent course of the case showed to be correct.

OTOLOGY

UNDER THE CHARGE OF

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Prognosis in Gunshot Wounds of the Ear and Report of a Case of Operative Removal of a Revolver Bullet from the Middle Ear with Preservation of the Hearing.—Notwithstanding the frequency of gunshot wounds of the temporal bone, since this is an accepted region for attack in attempts at suicide by means of fire-arms, the infrequency of reports of successful attempts at the removal of the incident projectile is due, according to LEWIN (*Monatsch. f. Ohrenheilk.*, xlvii, 6), to the fact, on the one hand, that the patient declines operation, or on the other, that the surgeon, in default of immediate danger to life, hesitates to undertake a difficult and critical operation. Before the contribution of Schwartz, in 1885, the opinion of Bergmann that a gunshot wound of the temporal bone was almost invariably fatal, because his careful search of the literature of the subject revealed only two exceptional cases, was that usually accepted, but Schwartz, five years after Bergmann's report, published a series of such exceptional cases and was followed with numerous similar contributions by other authors. Schwartz explained the exceptional cases upon the basis of the fact that the frequent backward pointing of the weapon resulted in the expenditure of the major force of the projectile upon the resistant posterior wall of the bony external canal and the mastoid process, rather than forward and inward toward the carotid artery and inward toward the sinus. Notwithstanding this preservative factor a fatal termination is by far the more common result of a rifle or a revolver wound in the area in question, and this liability is enhanced by the increased penetrative power of modern projectiles. In the majority of the fatal cases death is practically immediate though Preysing and Schwartz report a case in which the ultimate result followed the injury three and one-half years later in consequence of leptomenigitis, a circumstance in favor of Lewin's concluding argument that when the presence of a projectile in the middle ear is satisfactorily determined, the prognosis as to the ultimate result

must be a doubtful one until the foreign body has been removed. With the successful removal of the projectile the prognosis is improved and steps toward repair of the injury, and of the effect of the possible localized suppurative process, may be undertaken; in view of these considerations the fact of the presence of the projectile in the middle ear is sufficient ground for operative interference. Lewin's case was that of a man, aged twenty-six years, who reported that he had been wounded, in the left temporal region, two and one-half years previously, two balls from a bull-dog revolver having taken effect one in front of and the other behind, the left ear; he immediately lost consciousness and recovered to find himself in a military hospital where he remained two months and was then discharged well and returned to duty. During the two following years he was in good condition, except for impaired hearing and subjective noises in the left ear but at the end of that time there began, without untoward symptoms, a thin discharge from the left ear which soon became purulent and offensive, and had so continued up to the time of his examination, recently also there had been a swelling below the auricle and pain in the depth of the ear. The first ball had entered the ear in the region of the tragus and the second had taken lodgement in the soft cervical tissues, as shown by a scar $2\frac{1}{2}$ cm. below the auricle. The presence of the first ball in the depth of the middle ear was determined by objective and tactile examination and by means of radiography and confirmed by the radical operation that followed. This operation included an extensive removal of the surrounding bone, much of which had been splintered, in order to get adequate room for the removal of the projectile, the expansion of which had forced it upward to the tegmen tympani, backward to the mastoid antrum and the region of the horizontal semicircular canal and against the wall of the nerviduct of the facial, and likewise forward to the wall of the carotid canal; the drum-head and ossicles were absent. The subsequent progress of the cases was uneventful, at the end of two months dermatization of the cavity had been effected, there were no subjective symptoms, beyond a moderate circulatory tinnitus, and the hearing was improving, the voice in ordinary conversation tone being heard, in the left ear, at a distance of five meters.

A Fourth Crista Acustica.—BENJAMIN (*Zeitsch. f. Ohrenheilk.*, Band lxxviii, Heft 2-3, S. 101) describes the structural differences between the crista and the macula acustica and summarizes them, the crista being elevated, resting upon a fold of the membranous wall having long ciliate projections and lacking oboliths, the macula, on the contrary, presenting a flattened or depressed surface, the ciliate projections being short and the surface beset with oboliths, and follows with a careful review of the literature of the subject together with the result of his own observations, and a comprehensive summary. In the majority of vertebrates there is, in addition to the crista of each of the three ampullæ a fourth crista situated in the posterior sinus of the utricle in the neighborhood of the ampulla of the posterior, vertical canal. This Benjamin considers to be the so-called macula acustica of Retzius or macula acustica neglecta not at all a macula in the sense of the differentiation made by the author but veritably a

crista, occurring in the majority of the vertebrates, in the lower forms as a well developed fourth crista, in the higher as a more or less rudimentary organ. URBAN PRITCHARD, at the meeting of the Ninth International Otological Congress, demonstrated recently discovered extra nerve terminations in the ampulla in birds, their being, in some birds, in addition to the nerve epithelium of the crista acustica of the ampulla, large areas of similar nerve terminations lining the walls of the ampulla and the surfaces of the fan-shaped bodies described by Albert Gray. In a similar communication, at the meeting of the Seventeenth International Congress of Medicine, he refers to the work of McKenzie on the semicircular canals and sense of position or orientation and considers the importance of an extra acute orientation to birds for flying, especially to the migratory birds, as met by the larger areas of nerve terminations in the semicircular canals.

Improvement in Hearing after the Radical Operation by Use of an Artificial Drum-head.—In 49 cases with absence of the drum-head and dermatized surfaces throughout the middle ear, the majority of them successfully healed radical operations, GUTTICH-*(Passow's Beitrage, vi, 3)* endeavored to improve the hearing by means of the application of cotton artificial drum-heads soaked in paraffin inserted in the customary manner and allowed to remain at first from fifteen to thirty minutes, then gradually, for longer periods, up to eight or ten hours and in some instances continually for several days. The lesser resistance of an artificially dermatized surface to the influences of irritation and maceration demands more careful observation of conditions than would be needed in cases where the artificial drum-head rests upon a secreting mucous membrane. In 35 of the 49 patients tested by this application the hearing was not improved, or in so slight a degree as to make the gain practically valueless. In the remaining 14 cases there was marked improvement, in different degrees, but always accompanied by an extension of the lower tone limit and often a lengthened duration of hearing for the lowest tones; the especial value of the application in these cases being that the patients heard surrounding conversation not only from a greater distance, but more easily and better defined.

Primary Acute Mastoiditis.—DE SANTALO (*Archiv. International, 1913, xxxv, 1*). In a patient presenting the symptoms of an acute mastoiditis of six days' duration, fever, pain, tenderness upon deep pressure over the mastoid, edema and projection of the auricle, the external canal was filled with a mass of cerumen, the removal of which revealed a drum-head entirely normal in appearance, with exception of a moderate injection of the pars flaccida and of the manubrial plexus. An extensive incision of the drum-head was ineffectual so far as the liberation of contained discharge was concerned, the ear remaining dry, operative opening of the mastoid cavity was proposed for the following day. In the meantime an effort was made, by means of repeated warm instillations of cocaine and adrenalin solutions and cataplasms, to effect a decrease in the swelling of the mucous membrane of the aditus and outflow of the fluid, retained within the mastoid, through the antrum. During the night there

was an improvement in the symptoms and in the morning a copious purulent discharge from the ear containing *Staphylococcus aureus* occurred; five days later the ear was entirely healed. The infrequency of duly accredited cases of suppuration in the mastoid cavity without a corresponding suppuration in the middle ear makes this report of especial value, the infection having occurred, in de Santalo's opinion, from a diseased condition of the nose, through the tube and the tympanum, without infection until the antral mucosa was reached, when the incident swelling closed off the pneumatic spaces of the mastoid and permitted proliferation of the infection within that area only.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Air Emboli in the General Circulation.—BENEKE (*Centralbl. f. allgem. Path. u. Path. Anat.*, 1913, xxiv, No. 9) gave at the recent meeting of the German Pathological Association, a paper upon the occurrence of air emboli in the general circulation, apart from its existence in Caisson disease. It occurs, of course, relatively seldom, but may happen by the entering of air into the lungs through wounds of those organs. Many authors have considered the possibility of air making its way through the intact lung capillaries into the pulmonary veins in so great a quantity that sudden death has occurred by reason of its lodging in the arteries of the brain; it is necessary for such a happening that the intrapulmonary pressure should be extremely high. When such diffusion of air does occur, it is most often combined with interstitial emphysema, so that it is perhaps incorrect to speak of intact lung capillaries, although capillary hemorrhages in some of the experiments have not been seen. Beneke observed 4 cases of "foam" found in the heart and vessels, especially in the left auricle and left ventricle; 2 of these had occurred in newborn children with asphyxia at birth; in 2 other cases, there had been spasmodic deep breathing after a hemorrhage under the tentorium; 2 other cases referred to three months' old children with hemorrhage, in both of whom death had occurred suddenly, one with air embolism in the left auricle of the pulmonary artery, and the other with air embolism in the right heart, which apparently occurred by the passage of air from the general circulation. The existence of such cases as those in which there are emboli in some of the brain vessels demands that the section be made with the entire body under water. The suggestion is offered that some of the brain necroses of obscure origin arising in children during the first week of their age, showing themselves as large ischemic softenings or multiple small areas of calcification in the

brain following upon primary necrosis, may have originated through air emboli. The rapid absorption of air in such a locality would naturally occur, so that the exact diagnosis must remain doubtful. Beneke considers that from what is known about Caisson disease, it must not be considered that air emboli necessarily lead to rapid death; but that there may be definite local lesions occurring as a result, which become healed.

Formation of Bile Pigment from Hemoglobin.—WHIPPLE and HOOPER (*Jour. Exp. Med.*, 1913, xvii, No. 6) find as a result of their observations upon dogs, that hemoglobin can be changed into bile pigment in the circulating blood without the participation of the liver; in which case they think it likely that the endothelium of the bloodvessels is the agent. They injected, intravenously, red cells obtained from the animal injected and laked by distilled water. The change to bile pigment occurs in the same time in animals with normal circulation, in Eck fistula animals, and in animals with Eck fistula plus ligation of the hepatic artery. Even when the liver, spleen, and intestines have been shut out of the circulation, and in animals with head and thoracic circulation, bile pigment formation goes on as above. When normal and Eck fistula dogs are injected with hemoglobin from the animal's own laked red cells, hemoglobin appears in the urine in a few minutes, and bile pigment in from one to one and a half hours. If the portal blood be shut out from the liver, or if the liver blood supply be lessened by three-fourths, the reaction is unmodified. Hematogenous jaundice produced by chloroform anesthetic with a central liver necrosis occurs alike in the normal and the Eck fistula animal, and is considered by the authors to be partly due to capillary biliary obstruction, and partly to the formation of a hemolysin in the injured cells of the liver. Bile and bile pigment are formed less abundantly in an Eck fistula dog than in a normal animal, with less icterus, which is probably to be explained by the lessened activity of liver cells under a decreased blood supply. Bile pigment can scarcely, therefore, be formed solely from hemoglobin, because hemolysis is not more abundant in the normal than in the Eck fistula dog. Whipple and Hopper consider, therefore, that bile pigment formation depends rather upon the activity of the liver cells than upon the amount of hemoglobin supplied to them.

Diabetes Insipidus and Tumor of the Hypophysis.—BERBLINGER and GOLDZIEHER (*Centralbl. f. allgem. Path. u. path. Anat.*, 1913, xxiv, No. 9) have brought forward reports indicating the liability of tumors of the hypophysis to cause diabetes insipidus. The former reported a primary sarcoma which had grown extensively in the brain and had involved the stalk and the posterior lobe of the hypophysis; diabetes insipidus had arisen about six months before death. Goldzieher's first case had polyuria for six years, and at section there was found a dense fibrous semicircular tumor in the sella turcica, in which the chiasm was embedded. It consisted of fibrous tissue with granulation cells which by the inroad of lipoid had become xanthoma cells; the posterior lobe as well as the infundibulum was completely implicated; the anterior lobe, with the colloid

retained in the intermediate zone, remained unchanged. His second case, again one of true diabetes insipidus, died by reason of a carcinoma of the lung. The hypophysis though unchanged to the naked eye, showed microscopically a cystic adenoma of the intermediate zone, and serial sections showed that there was a definite pressure upon the intermediate lobe. When one considers with such case reports of diabetes insipidus, the existence of changes that have been observed in the adrenals, and the various forms of dystrophy which have been frequently described, it is realized that we are probably dealing with a disease of very complex etiology concerned with the functions of the ductless glands.

Experiments with Blood Serum and Cerebrospinal Fluid of Epileptics.—TREVISANELLO (*Centralbl. f. Bakt. Parasitenk. u. Infektionskr.*, May 23, 1913, Band lxix, Heft 3) undertook the injection of blood serum and cerebrospinal fluid from epileptics under the dura of guinea-pigs. His results showed that in a series of experiments, if the blood serum of an epileptic was injected into a guinea-pig, and after eight, ten, or twelve days the cerebrospinal fluid of the same patient was similarly injected, anaphylactic phenomena resulted, consisting of convulsions, subnormal temperature, and sometimes death. It mattered not whether the cerebrospinal fluid or the blood serum was injected first. He found that the anaphylactic reactions appeared more quickly, and were more pronounced if the patients from which the fluids were taken, were the subjects of frequent and lasting epileptic crises, than if they were less so. The same result was obtained whether the fluids were taken immediately after an epileptic attack, or after the lapse of time. Trevisanello's experiments were properly controlled. The blood serum of epileptics followed by cerebrospinal fluid gave the results above noted, and in the fatal cases no pathological changes were found at autopsy. The symptoms came on within a few minutes after the second injection had been given, and lasted sometimes as long as an hour. None of the experiments so conducted failed to show this result. In the groups of animals, however, in which epileptic serum was followed by non-epileptic cerebrospinal fluid, or non-epileptic cerebrospinal fluid followed by epileptic serum, there were no results. In the groups of animals where non-epileptic serum and non-epileptic cerebrospinal fluid were used under the same circumstances, no effects upon the animals were observed.

Typhoid and Antityphoid Serum.—ANDRIESCU and CIUCA (*Annal. de l'Inst. Pasteur*, Tome xxvii, No. 2) have been able to test Besredka's serum by giving it in large doses to 17 severe cases of typhoid fever, in which the diagnosis has been established by the serum reaction and the finding of bacilli in the blood. The serum was given hypodermically, and sometimes in very grave cases by the veins; once it was administered by the mouth throughout five successive days. As soon as the sick became convalescent, Andriescu and Ciuca made repeated bacteriological examination of the stools for the purpose of determining if bacilli were or were not being secreted by this road. The bacilli disappeared from the circulation very quickly after the injection of serum, and they have not been able to get a single instance

of blood culture in any case after it had been administered. The disappearance of the bacilli from the stools is also prompt and complete. They have not found any direct result upon the course of the fever, but consider there is a marked amelioration of the health. Among 17 cases so treated, all severe examples of the disease, only 1 has proved fatal. Bacteriolysis may be so rapid, and so slight a quantity of endotoxin may be thrown out that there may be an eruption of sterile scattered abscesses. Andriescu and Ciuca are unable to say whether the source is anti-endotoxic, or is merely bacteriolytic, nor have Pfeiffer and Bessau been able to discover the answer to this question.

Streptococcus in Rheumatism.—BEATTIE and YATES (*Proc. Path. Soc. Great Britain and Ireland*, January 3-4, 1913) examined 129 cases of various infective maladies, taking their cultures most frequently from the synovial membranes. Forty-eight of these yielded the streptococcus, and of these 48, 32 had a history of recent rheumatism. From these 32 cases of recent rheumatism, 31 inoculations were made into rabbits, yielding in 1 case septicemia, and in 19 cases arthritis; 11 cases showed no result; of 8 samples of streptococci from non-rheumatic cases, 7 times septicemia occurred, and once arthritis. In 12 human cases that they examined during the active process of rheumatic fever they obtained three positive results, of which each strain produced arthritis in the rabbits experimented upon.

The Cultural Reactions of the Typhoid-coli Group.—EMYRS-ROBERTS (*Proc. Path. Soc. Great Britain and Ireland*, January, 1913), experimenting on certain well-known tests used to differentiate bacillus typhosus and *Bacillus coli*, considers that 10 per cent. peptone water is superior to 1 per cent. for the indol reaction; that the chloroform indol reaction will not differentiate strains of *B. coli*; that boiling after the addition of the reagents in the indol test intensifies the reaction; and that the neutral red reaction is unsatisfactory. Ten per cent. lactose added to litmus milk hastened the acid and clot reaction for *B. coli*, and for organisms producing a permanent alkalinity, after a transient acidity, the ordinary litmus milk is preferable. Emyrs-Roberts also considers that 15 per cent. lactose litmus broth is extremely valuable, in differentiating closely allied organisms of the colon group one from another.

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THE
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ORIGINAL ARTICLES

THE CLINICAL FEATURES OF CASES OF SUBACUTE BACTERIAL
ENDOCARDITIS THAT HAVE SPONTANEOUSLY
BECOME BACTERIA-FREE.¹

By E. LIBMAN, M.D.,

NEW YORK.

At the meeting of the Association of American Physicians in 1912, the writer² presented a paper on the results of a study of the endocardial lesions found in cases of subacute bacterial endocarditis (chronic malignant endocarditis, chronic infectious endocarditis, chronic ulcerative endocarditis, endocarditis lenta). After describing these lesions he presented evidence that the bacteria in such cases could spontaneously disappear from the lesions and that the lesions could heal in part or entirely. It was shown that the healing of the lesions was not necessarily accompanied by recovery from the clinical standpoint. There are two reasons for this. In the first place the healing of the lesions leaves fibrous and calcareous tags or masses, which interfere with the usually already improper functioning of the valves and the musculature of the heart, and which may give rise to embolic phenomena. In the second place so much injury may be done to the kidneys and the blood-forming organs that although the bacteria disappear the damaged tissues cannot functionate to the extent necessary for the preservation of life.

In the paper referred to there were briefly presented notes on eleven cases, concerning which there was no doubt that the patients

¹Read at the meeting of the Association of American Physicians, Washington, D. C., May 8, 1913.

²Libman, AMER. JOUR. MED. SCI., September, 1912, cxliv, 313; Trans. Assoc. Amer. Phys., 1912, xxvii.

had suffered from subacute bacterial endocarditis and had spontaneously become bacteria-free. In three of these cases (these were the earliest cases) the condition was not suspected clinically, and the diagnosis was established by the evidence accumulated by a study of the postmortem material. In the other cases the diagnosis was made from the clinical features and proved by bacteriological and pathological investigations. The presence of the embolic glomerular lesions in the kidneys, described by Loehlein, and later by Baehr³ and Gaskell, we found to be pathognomonic of the existence of subacute bacterial endocarditis when due to the cocci usually found in such cases. In those cases which were due to the influenza bacillus, such lesions were not found. As these cases are quite infrequent, this is not evidence that such lesions cannot be produced by subacute or chronic endocarditis due to this organism.

It is my present purpose to give a short review of the clinical features of the bacteria-free cases that we have observed up to the present time. As it would not be possible, except in monographic form, to discuss these cases in detail, only certain important points will be mentioned. There will be appended a short description of the clinical course of each of the cases which were utilized in the course of the study.

In the earlier paper the following description was given of the clinical course of the cases seen up to that time:

1. They may develop a nephritis and die of uremia.
2. They present the picture corresponding to what we have been wont to call chronic endocarditis with fever (that is, they have a valvular lesion, more or less fever from time to time, usually low, occasional petechiæ, occasional joint symptoms, and embolisms). Some of these cases resemble cases in which bacteria are demonstrable in the blood. Some are pale, others more or less pigmented.
3. Some of the cases present a complex that appears to have been entirely overlooked. The striking feature is a peculiar diffuse brown (*sometimes quite dark*) color of the face. The rest of the body may show some pigmentation. There is evidence of a valvular lesion, there is more or less anemia, usually a palpable spleen, and usually also tenderness of the sternum. The patients feel weak and do not sleep well. Petechiæ occasionally occur. There is fever from time to time, usually low. Erythrocytes are found in the urine in some of the cases. The subsequent history of such cases is not yet known; one case died with symptoms of cerebral embolism. The important feature of these cases is the curious change in the color of the face. Since I have observed it in bacteria-free cases, I have looked for it in cases in the bacterial

³ AMER. JOUR. MED. SCI., September, 1912, cxliv, 327.

stage, and, to my surprise, I find that while the faces of most of the cases are sallow, or of a rather white color, some develop a certain amount of brown or café-au-lait color.

4. They may go on with more or less anemia, and suffer from that and from decompensation.

In discussing the splenic enlargement which occurs in the bacteria-free as well as in the bacterial stage, I suggested that from observations made several years before, I had reason to believe that a case would occasionally be found in the bacteria-free stage in which marked enlargement of the spleen might be a very conspicuous feature of the case. I suggested that when such a case did come under observation, it might be regarded as a case of Banti's disease plus chronic valvular disease, and that it might not be recognized that the case was really one of subacute bacterial endocarditis in the bacteria-free stage, with marked enlargement of the spleen as the most conspicuous feature. During the last year I saw a case which showed that such a clinical picture is possible. A description of it is appended (Case XXI).

I have given the classification which I described in the paper published last year, because it is the basis of my present classification. After describing the mode of onset, the symptoms, and the termination of the cases in the bacteria-free stage, I shall show in what way I have found it necessary to modify the classification.

The remarks which follow are based on a study of 21 cases of subacute bacterial endocarditis in the bacteria-free stage; 4 of the cases are still alive. Postmortem examinations were made in 17 of the 18 cases that succumbed, and in all there was ample proof from the clinical, bacteriological and pathological studies that we were dealing with the disease under discussion. In the course of the investigations, 1 case was encountered which was suspected of being in the group, but there was not sufficient evidence present at the postmortem examination to corroborate the clinical suspicion. This case is mentioned among the appended notes, but is not described in detail. It will be of service on another occasion when the question of differential diagnosis is taken up. Up to May, 1910, the writer had observed 43 cases of subacute bacterial endocarditis.⁴ Since that time he has made more or less comprehensive studies of 82 more cases, the entire number being 125. Of the 82 cases seen since May, 1910, 18, or over one-fifth, were in the bacteria-free stage (1 case became bacteria-free under observation, Case VIII). The writer is convinced that a careful study of all the cases of chronic valvular disease seen at the hospital during that period would have resulted in unearthing a larger number of cases. It is only by a careful scrutiny of all cases supposed to be instances of uncomplicated chronic valvular disease that one becomes im-

⁴ Cf. Libman, AMER. JOUR. MED. SCI., October, 1910.

pressed with the frequency with which patients are found suffering from chronic valvular disease plus the bacteria-free stage of subacute bacterial endocarditis.

We will now proceed to a review of some of the clinical features of the disease:

DURATION. This is difficult to estimate, as most of the cases were not seen in the bacterial stage, and therefore one can have no idea of the length of the bacteria-free periods. In Case VIII, in which influenza bacilli were found for almost two months, the later bacteria-free period was about four months. There is sufficient evidence to show that the bacteria-free period may last for two and a half years, as in Case XIII. In two cases there was a history of the presence of cutaneous tender nodules three (Case XX) and three and a half years (Case XIII) before death. It is to be remembered that there are a few records in the literature of cases in which patients became bacteria-free under observation and remained well except for the presence of the previously existing valvular lesion. But the period of observation in these cases was not very long when the cases were reported, and no later reports have been issued which state whether the patients developed any of the special features to which we have drawn attention as occurring in the bacteria-free stage.

PREVIOUS HISTORY. In one case there was a history of scarlet fever at an early age. In a number of cases there was a history of previous attacks of rheumatism and of the establishment of a valvular lesion. In some cases the patients had suffered for a longer or shorter time from palpitation, dyspnea, pain in the precordial region, and cough with or without expectoration; at times the sputum was hemorrhagic.

In a few of the cases there was a history of an attack of fever, pains in the joints, palpitation, and dyspnea a number of months before the development of the symptoms for which the patient came under observation. It is proper to suspect that these attacks in some instances represent the bacterial stage of the disease. A critical analysis of the data bearing on this point will be submitted at another time.

MODE OF ONSET. In most of the cases the early symptoms were cardiac in nature. There was dyspnea, palpitation, and cough with or without hemorrhagic expectoration. With these symptoms there might or might not be chilly sensations, fever, sweats, joint pains, and swelling of the legs. In one case severe pain in the thigh was the first symptom (due to an embolic aneurysm of the femoral artery). In another a severe pain in the sacral region was the prominent early symptoms (this is at times observed also in the bacterial stage of the disease). Vomiting associated with headache and dizziness was the initial symptom-complex in a couple of cases; in one case epistaxis, and in another purpura first appeared. Frequency

of urination was a striking symptom that appeared early in two cases.

FEVER. The temperature in the bacteria-free cases does not run as high as in the bacterial cases. It may be high in cases that are seen, apparently, shortly after the bacterial stage has ended, or if complications develop or an intercurrent disease. Embolisms may cause marked rises of temperature, and at times chills, even though there be no bacteria in the pieces thrown off from the valves. In many cases the temperature is practically normal during almost the entire period of observation.

VALVULAR LESIONS. In every one of the cases there was evidence of an organic lesion of the mitral or aortic valve, often of both. As a rule no new murmurs developed during the disease.

RENAL PHENOMENA. This subject is so important in connection with the symptomatology of the bacteria-free stage of subacute bacterial endocarditis that it is possible to give only the shortest account of our observations. Macroscopically, hemorrhagic urine usually occurs either when the case comes under observation shortly after the bacterial stage is ended (as made apparent by the clinical pictures or by the study of the age of the vegetations found in the heart) or as the result of gross embolic lesions of the kidney. Erythrocytes in small numbers are found in the urine in a number of the cases, but not with the regularity or persistence with which they are found in the bacterial stage of the disease.

Albumin and casts are found in some of the cases from time to time. In others there is definite evidence of a more or less marked progressive disease of the kidney. In this latter group of cases there are two types. In the one there is passed a subnormal, normal, or increased quantity of urine of a normal or subnormal specific gravity, albumin and formed elements being more or less conspicuously present. In the cases of the second type there is passed a large amount of urine (up to 2700 c.c.), with a high specific gravity (up to 1028 or 1032), and this may occur even when there are present but a few formed elements and only a trace of albumin. This second clinical type of renal disturbance has not, as far as the writer knows, been previously described. The relationship of the clinical phenomena and the pathological lesions is worthy of a special study.

Symptoms due to renal insufficiency were prominent in a number of cases; in some they dominated the clinical picture. In one case (Case III) the examination of the fundus revealed edema of the optic disks and retina. As will be seen later, renal insufficiency was the main cause of death in a comparatively large number of cases.

BLOOD CHANGES. In the cases in which examinations were made (and they were made in nearly all) there was found a more or less marked anemia, always of the secondary type. The hemoglobin

in some cases was as high as 65 per cent., and in others as low as 35 or even 20 per cent. There was a tendency to progressiveness in the anemia in many of the cases. Nucleated erythrocytes were never found. The bone-marrow of the femur was examined in two cases, and was found to be dark red in color, and to show typical regenerative changes. In a third case the tibia was examined and fatty marrow found.

When the anemia was profound it was plainly revealed by the color of the skin and mucous membranes, and by a general edema most marked in the lower limbs.

The leukocytes were usually not increased in number except when complications ensued. In some cases the number diminished during the course of the disease (to 4000 at times). The polymorphonuclear cells were either normal or moderately increased (barring periods during which there were complications). In a few cases they diminished during the progress of the disease (in one case to 36 per cent.).

SPLENIC ENLARGEMENT. The spleen was palpable in all the cases except four. At times it was enormously enlarged. In all the cases but one of those in which the spleen was not palpable it was found enlarged at the postmortem examination, at times very much so. In a large percentage of the cases the Malpighian bodies in the spleen were conspicuously enlarged and, microscopically, hyperplastic.

PETECHIÆ. These were found at one time or other in 13 cases. They were located in the mucous membranes (especially the conjunctivæ) and the skin. As a rule few were found as compared with the number seen in cases in the bacterial stage.

PURPURA. This was noted in three cases. In one it was the main symptom for two months before the patient came under observation. In another case it occurred repeatedly throughout the course of the disease.

TENDER CUTANEOUS NODULES. These were found in only three cases. In two they persisted close up to the time of the fatal termination. One of these two patients had had these lesions for three years, and one for three and a half years.

STERNAL TENDERNESS. This symptom, as the writer stated last year,⁵ seems to be more marked in the bacteria-free stage than in the bacterial stage. It was found in all of the cases in which it was looked for. In one case the tenderness of the lower sternum was so marked that it was elicited by the lightest tap. The long bones were usually not found tender.

SWEATS AND LOSS OF WEIGHT. These symptoms were not nearly as marked as in cases in the bacterial stage. In only a few cases is there a note of profuse perspiration. That loss of weight should not be a prominent symptom is evident from the fact that many

⁵ Trans. Assoc. Amer. Phys., 1912.

of the cases have comparatively little fever as compared with cases in the bacterial stage.

PIGMENTATION. The brown color of the face was noted as a striking symptom in nine cases. In some of these it increased under observation. A few of the anemic patients whose faces were at first white, later developed a more or less marked café-au-lait tint. This has also been observed by the writer, as stated in a previous publication, in the bacterial stage, but the development of a marked brown color he has seen only in cases in the bacteria-free period.

PAINS. The only pains that occurred with any frequency were joint pains. These occurred particularly in the cases in which purpura was a symptom. Reference has already been made to the case in which pain in the sacrum was a marked feature. Pains due to various complications need no discussion here.

ANEURYSMS. Apart from the occurrence of aneurysms of the mitral valve, the septum membranaceum, and the sinuses of Valsalva, which produced no recognizable symptoms, there was encountered once an embolic aneurysm of the femoral artery. The aneurysm had ruptured into the soft parts and had eroded the bone. The patient was sent into the surgical service of the hospital with a diagnosis of osteomyelitis, because of the rapidly developing large tender swelling, the fairly high temperature, and the high leukocyte count with polynucleosis. Because of the presence of a valvular lesion, a large spleen, and a marked anemia, I suspected that we were dealing with a case of subacute bacterial endocarditis. Further observation proved that this view was correct. The post-mortem examination corroborated the clinical opinion; the lesions were practically bacteria-free, and for the main part organized. This was in keeping with the fact that the three blood cultures made in the case gave a negative result.

CARDIAC SYMPTOMS. These can be classed in two groups. We must consider first the subjective and objective symptoms due to the valvular lesion as such. Here we include the palpitation, pains in the chest, dyspnea, cough and expectoration, congestion of the viscera, edema of the legs, and hemorrhagic infarction of the lungs.⁶ All these symptoms may occur in any case of valvular disease.

In the second group we include the embolisms, petechiæ, purpura,⁷ embolic aneurysms, and tender cutaneous nodules; this second group of symptoms occurs when there are friable masses on the valves of the heart or on the wall. They are therefore common events in cases of subacute bacterial endocarditis in the bacterial or bacteria-free stage, and may well be called endocarditic symp-

⁶ These are due oftener than is generally supposed to thromboses in veins of the lower extremities or of the pelvis.

⁷ This could, of course, at times be due to a hemorrhagic diathesis.

toms. Cerebral embolism seems to be as frequent an occurrence in bacteria-free as in bacterial cases.

JOINT SYMPTOMS. These are much less common than they are in the bacterial stage. There may be joint pains or joint swellings, or both. Occasionally, as stated above, purpura is also present. The joint swellings are, as a rule, not marked, and are quite transitory. The writer does not remember having seen a joint that was tender or over which the skin was red.

CAUSE OF DEATH. The cause of death can be fairly definitely stated in 16 of the fatal cases: In 3 it was due to cerebral embolism, in 4 to uremia, in 2 to the progressive anemia and an intercurrent pneumonia, in 1 to uremia, embolism, and pneumonia, in 1 to pneumonia, in 3 to cardiac insufficiency, in 2 to progressive anemia, with concomitant cardiac weakness. To put the matter in another way, it may be said that cerebral embolism was a determining factor in 4 cases, uremia in 5 cases, intercurrent pneumonia in 4 cases, anemia in 4 cases, and cardiac insufficiency (unaccompanied by profound anemia) in 3 cases.

The important role played by the progressive anemia, the nephritic changes, the presence of vegetations on the valves, and the improper functioning of the valves and musculature of the heart is thus made very clear.

The lesions found in the heart in all the cases were, in the main, of the same type as those described in the writer's earlier paper on this subject. In two cases atypical lesions were found, the main feature of which was a peculiar worm-eaten appearance of the mitral valve, which in both instances was the seat of an old mitral stenosis (Cases XIII and XX). In one of these two cases the glomerular lesions were of a diffuse type and the typical embolic lesions were not present. The clinical history was, however, quite typical, and the characteristic tender cutaneous nodules were seen by the writer.

GENERAL GROUPING OF THE CASES. From the description which we have just given of the symptomatology of the disease under consideration it might appear that most of the cases look quite alike clinically. But while it is true that petechiæ, sternal tenderness, a palpable spleen, and a more or less marked anemia occur in most instances, the cases can be grouped according to certain features that particularly impress the observer. In the earlier part of this paper the writer quoted the classification of the cases that he attempted to make and which he presented last year, and he also drew attention to the occasional occurrence of an unusual enlargement of the spleen. The study of the additional cases seen since then, in conjunction with a review of the earlier cases, leads him to describe five prominent features, one or more of which may be found in a certain case, and characterize the case rather than describing four or five groups; for he has found there are cases

that belong to more than one of the groups which he described last year.

The five prominent features which may be found are:

1. Marked progressive anemia.
2. Brown pigmentation of the face.
3. Marked evidence of renal disease.
4. Marked enlargement of the spleen. The spleen may be so enlarged that the case may be considered a case of chronic valvular disease associated with Banti's disease.

5. Phenomena due to the vegetations present on the valve. These are what I term endocarditic symptoms. They consist of more or less elevation of temperature occurring from time to time, petechiæ, occasional joint symptoms, and embolisms.

Whenever any of these clinical features are found in a case of chronic valvular disease it is of the greatest importance, for it draws attention to the possibility that the case is one of chronic valvular disease plus subacute bacterial endocarditis in the bacterial or bacteria-free stage.

Afebrile or nearly afebrile periods of fair duration (several weeks) or negative results of blood-cultures would help make the differentiation between the two stages.⁸ The diagnosis from certain cases of acute rheumatic infection of a valve previously the site of disease, and from some other conditions may present difficulties. The writer will not discuss this question, as it is his purpose at the present time to describe clinical features and not differential diagnosis. All he wishes to state now is that studies made by Dr. D. J. Kaliski and Dr. P. Aschner have not demonstrated the value of complement fixation tests as an aid in the diagnosis of bacteria-free cases.

In the appended description of our cases, summaries are given which show which of the five important features of the bacteria-free cases occurred in each. A few examples will, however, be of interest here:

Case I. Pigmentation; endocarditic symptoms.

Case III. Nephritic symptoms.

Case V. Endocarditic symptoms; progressive anemia.

Case VI. Endocarditic symptoms; intense anemia; pigmentation.

Case XV. Pigmentation.

Case XXI. Marked splenic enlargement; progressive anemia; renal symptoms.

DESCRIPTION OF CLINICAL COURSE OF CASES. In the following notes there will be presented a concise description of all the cases

⁸ It is an interesting fact that in cases of subacute bacterial endocarditis in the bacterial stage, bacteria can practically always be found in the blood if the temperatures are not elevated a great deal. It is in the cases with high temperatures and with very marked oscillations that one fails at times to obtain bacteria in the blood cultures although the bacteria are present in enormous numbers in the vegetations in the heart.

of subacute bacterial endocarditis in the bacteria-free stage that the writer has observed. As the cardiac lesions were described rather fully in the paper presented before the Association last year, and as it is his purpose at another time to publish an account of these lesions in greater detail, he will, in the descriptions of the cases, refer to the postmortem findings in as brief a manner as possible. The renal lesions will also not be described at the present time, as they will form the basis of another communication. It is sufficient to state that in nearly all the cases the embolic glomerular lesions, which are characteristic of the disease (except when due to the influenza bacillus), were present. In a few cases these embolic lesions were associated with other diffuse glomerular lesions. In a few cases only diffuse lesions of the glomeruli were present. These lesions will be described at another time. In the few cases in which embolic lesions were not present, there was sufficient evidence present clinically (tender cutaneous nodules) or at the postmortem examination to put the cases into the group which the writer has termed subacute bacterial endocarditis in the bacteria-free stage.

A perusal of the following notes will show that the writer has included four patients who are still alive, all of whom are in quite good condition. Although the absolute evidence of the fact that they belong in this group is not forthcoming, the cases are so typical clinically and correspond so closely to other cases in which the clinical diagnosis was proved correct by postmortem examination that it seemed desirable to include them.

CASE I.—Observed from July 2, 1905, to August 6, 1905. Three blood-cultures were made, with negative results. There was a previous history of scarlet fever at the age of two years; pains and redness of the joints during the last winter. Onset one month before admission, with cough and expectoration, cardiac palpitation, dyspnea, pain in both knees, which were red and not swollen. The heart showed evidences of an aortic lesion. The face was markedly pigmented. The spleen was palpable and petechiæ were present. An embolic aneurysm of the iliac artery developed. The patient passed large amounts of urine, up to 2000 c.c. a day, containing a moderate number of leukocytes and hyaline casts. The leukocyte count varied from 6200 to 9200; hemoglobin, 65 per cent., later 61 per cent. The temperature rose at the highest to 101° or 102°, except just before the embolism occurred, due to which the aneurysm developed; at that time the temperature was 104°. The cause of death was apparently a cerebral embolism. Postmortem examination revealed a healed clacareous bacteria-free lesion⁹ of the aortic valve, with an aneurysm of the mitral valve and fibrous lesions of the chordæ tendineæ. The spleen was

⁹ This means that the cultures from the centre of the vegetations showed no bacteria, and that smears made from crushed vegetations also showed no organisms.

large and showed marked hyperplasia of the Malpighian corpuscles and one infarction. In the kidney there was an embolic aneurysm.

SUMMARY. The main features in this case were pigmentation and endocarditic phenomena (development of non-bacterial embolic aneurysms).

CASE II.—Observed from May 1, 1907, to October 3, 1907. There were two blood-cultures, with negative results. There had been cardiac palpitation and dyspnea for six months. For two months prior to admission, attacks of purpura, and for five weeks edema of the legs, were present. The cardiac lesion was apparently aortic insufficiency. The spleen was palpable just below the free border of the ribs and petechiæ were present. Perspiration was a marked feature. The urine varied in amount from 750 to 850 c.c. Specific gravity ranged from 1008 to 1012; erythrocytes were present, also hyaline and hyalogramular casts. Blood examination at first showed 5200 leukocytes, 53 per cent. hemoglobin, and 3,040,000 erythrocytes. Later the leukocyte counts varied from 4000 to 7000; the polymorphonuclear count was as low as 41 per cent., except a short time before death, when it was 68 per cent. The hemoglobin dropped to 38 per cent. The temperature was usually around 100°, occasionally 101°, except when an embolism occurred or when a purpuric rash developed. Death was due to cerebral embolism. The autopsy showed a calcareous lesion of the aortic valve and an aneurysm of the membranous septum. The spleen was almost twice the normal size, contained old and recent infarctions, and the Malpighian bodies were prominent. Areas of softening were found in the brain.

Summary. The important features of this case were endocarditic phenomena (embolisms and purpura), the marked enlargement of the spleen, the urinary phenomena, progressive anemia, and lymphocytosis.

CASE III.—Observed from November 9, 1905, to May, 1906, and again from October 3, 1909, to November 3, 1909. There was one blood-culture, with negative result. A history was obtained of rheumatism occurring two years before the date of the first admission. During the first stay in the hospital there were joint symptoms and a pericarditis. Hemoglobin was 86 to 90 per cent., but progressively dropped to 65 per cent. The temperature was at first up to 103°, afterward practically around normal, except with occasional rises to 101° or 101.2°. The quantities of urine varied from 620 to 1600 c.c. The specific gravity varied between 1008 and 1028, being usually around 1010 to 1020; there was present a faint trace of albumin, and occasional hyaline and hyalogramular casts. The spleen was not palpable. There were evidences of mitral insufficiency. On admission the second time the patient gave a history of having developed edema of the legs five weeks before. Ophthalmoscopic examination showed marked edema

of the optic disks and surrounding retina. Hemoglobin dropped to 36 per cent. Urine quantity varied at first from 1300 up to 3000 c.c., and later dropped to 330 c.c. At the time of the second admission the urine contained a trace of albumin, numerous hyaline and granular casts, and leukocytes; later it was reddish brown in color, contained a heavy trace of albumin and numerous erythrocytes. The patient died of uremia. At autopsy there was found a fibrous lesion of the wall of the left auricle and fibrous and calcareous lesions of the chordæ tendineæ. The spleen was one and a half times the normal size.

Summary. The main features of this case were the progressive anemia and the renal phenomena.

CASE IV.—Observed from April 24, 1910, to May 9, 1910. There was one blood culture, with negative result. The patient had been dyspneic for one year. For two weeks there was vomiting, headache, and dizziness. There was evidence of mitral and aortic insufficiency; the spleen was palpable. There were no petechiæ. The patient looked anemic. Hemoglobin was 60 per cent.; leukocytes, 13,000; polymorphonuclears, 65 per cent. The urine varied in specific gravity from 1010 to 1013; there was present a faint trace of albumin; occasional hyaline casts, erythrocytes, and granular casts. The temperature was never over 102°, usually between 99° and 100°. The patient died of uremia, cerebral embolism, and a terminal pneumonia. The autopsy showed old pericardial adhesions and a lesion of the wall of the left auricle and of the chordæ tendineæ, which was almost entirely healed. The spleen was one and a half times the normal size, and contained infarctions.

Summary. Renal phenomena, old pericarditis, moderate anemia.

CASE V.—Observed from July 14, to October 8, 1910. There were three blood cultures, with negative results. There was a history of articular rheumatism at the age of six years, and of palpitation and dyspnea since that time. The onset of the present illness occurred ten weeks before admission to the hospital, with pain in the thigh, swelling, and limping, all this being due to a ruptured embolic aneurysm of the femoral artery. The heart showed evidences of mitral and aortic insufficiency. The spleen was large (the spleen was particularly large in view of the fact that the boy was sixteen years of age and much undersized). There was a café-au-lait color to the face. The urine at first showed a specific gravity of 1020, later 1004 up to 1020; there were present erythrocytes and hyalogramular and granular casts. The blood count showed 15,200 leukocytes; 65 per cent. polymorphonuclears and a hemoglobin content of 20 per cent.; later the leukocyte count was 8400; polymorphonuclears 36 per cent., and the hemoglobin dropped to 17 per cent. The temperature was usually up to 102°. Death occurred from progressive anemia and a terminal

pneumonia. The autopsy showed lesions of the mitral valve, chordæ tendineæ, and auricular wall, most of which were healed. In one part of the lesion there were found a few poorly staining cocci. The spleen weighed 510 grams (17 ounces); Malpighian bodies large.

Summary. Embolic aneurysm; marked splenic enlargement; renal phenomena; progressive anemia.

CASE VI.—Case observed from June 26, 1911, to April, 1912. There were nine blood-cultures, with negative results. There was a previous history of rheumatism. The onset occurred three months before admission, with increase of a previously existing palpitation and dyspnea. There was frequent urination. The heart gave evidence of an aortic lesion. There was marked pigmentation of the face. The spleen was palpable. Numerous petechiæ occurred often. There were hemorrhages from the gums. There were tender nodes on the hands and feet on August 30 and October 4, and even as late as March 1. The lower sternum became distinctly tender under observation. The urine was at first grossly bloody, later erythrocytes were found microscopically from time to time. The specific gravity varied from 1020 to 1022; the amounts of urine were from 1100 to 2400 c.c. The blood-examination showed a hemoglobin content of 39 per cent. at first; this then dropped somewhat lower, and a transfusion was done and the hemoglobin brought up to 55 per cent. It then rose to 61 per cent., but later dropped again. Leukocyte count was 10,400; polymorphonuclears, 81 per cent. The temperature was at first 101° to 102°, and later was occasionally as high as 101°, except just before crops of petechiæ developed. Death was due to progressive anemia and a terminal pneumonia. At the postmortem examination there were found calcareous and fibrous lesions of the aortic valve and aneurysms of the sinuses of Valsalva. The spleen was one and a half times the normal size; there was marked enlargement of the Malpighian bodies. The bone-marrow of the femur was red, and microscopically there were evidences of regeneration.

Summary. Pigmentation; renal phenomena; progressive anemia; tender nodes present long after the active stage of the disease was passed; hemorrhagic tendency; endocarditic symptoms.

CASE VII.—Period of observation from April 16, 1911, to June 13, 1911. Cultures of the blood were not made during life, but at the postmortem examination the blood was found free from bacteria, as were also the cardiac lesions. There was a previous history of acute articular rheumatism and of cardiac disease. The patient suffered from dyspnea, pain over the heart, cough, and hemoptysis. The present illness began two weeks before the date of admission, with dyspnea, orthopnea, pains about the heart, cough, and expectoration, which was at times hemorrhagic. Examination showed insufficiency of both aortic and mitral valves. Spleen not

palpable. No petechiæ. Urine showed a specific gravity of 1020 to 1026, and contained a trace of albumin. The quantities varied from 1400 to 1900 c.c. The temperature was usually up to 101° or 101.2°, later at one time up to 102°. The patient developed uremia and died suddenly, the explanation of the sudden death being unknown (the writer did not observe this case himself). At the postmortem examination there was found an adherent pericardium and a bacteria-free and partially healed lesion of the chordæ tendineæ, mitral valve, and auricular wall. The spleen weighed 570 grams (19 ounces), and contained infarctions.

Summary. Renal phenomena; marked splenic enlargement.

CASE VIII.—Period of observation from July 17, 1911, to October 14, 1911. In this case the first five blood-cultures gave growths of the influenza bacillus, three later ones remained sterile, the first of the latter being taken on September 9. The patient was told two years before the onset of the present illness that he had endocarditis. For eighteen months he had had pain in the ankles and feet, and had lost weight. On admission he complained of throbbing in the head, fever, and weakness. There were evidences of aortic insufficiency and mitral stenosis. At first the spleen was felt two fingers below the free border, and later four fingers below the free border. Petechiæ were present. The specific gravity of the urine varied from 1008 to 1024, later from 1011 to 1020; erythrocytes and hyaline and granular casts were present. Blood-count showed leukocytes, 6800; polymorphonuclears, 75 per cent.; hemoglobin, 64 per cent.; later the hemoglobin was 71 per cent, leukocytes 5800, and polymorphonuclears 42 per cent. The patient left the hospital some time after the blood was bacteria-free, and developed a marked progressive anemia and hydremia. At first the temperature was 104°, later not above 102°. The patient died of progressive anemia and exhaustion. An autopsy was not permitted.

Summary. Influenza bacillus infection; the case later became bacteria-free; progressive anemia; marked enlargement of the spleen.

CASE IX.—Period of observation from August 8, 1911, to August 24, 1911. Two blood-cultures were taken, with negative results. The patient had previously been in the hospital from September 24, 1910, to October 15, 1910. On the first admission there was a history that the patient had had rheumatism since he was fifteen years old. Six months before the day of the first admission the patient was taken sick with fever and pain in various joints. He had marked sweats, occasional dyspnea, palpitation, and pain over the heart. The face was of a brownish color. Examination of the heart revealed mitral insufficiency and aortic insufficiency. The spleen was palpable one and a half fingers below the free border. Petechiæ and purpura both occurred. The lower

sternum was distinctly tender. Urine showed a specific gravity of 1018 to 1020, a faint trace of albumin, some hyaline casts, and a few leukocytes. Blood examination at first showed leukocytes, 11,000; polymorphonuclears, 74 per cent.; later blood count showed leukocytes, 6000; polymorphonuclears, 74 per cent. On the day of admission the temperature was 103°, but after that did not rise above 100°. The patient died of cardiac insufficiency and uremia. Postmortem examination showed a bacteria-free calcified and ulcerative lesion of the aortic valve. The spleen weighed 210 grams (7 ounces); old infarctions were present; Malpighian bodies were prominent.

Summary. Pigmentation; endocarditic symptoms.

CASE X.—Period of observation from November 27, 1911, to January 31, 1912. Three blood-cultures remained sterile. Patient was taken sick, three weeks before admission, with dyspnea, cardiac palpitation, and nocturnal frequency of urination. There was marked brown pigmentation of the face. Examination of the heart revealed insufficiency of the aortic and mitral valves. The spleen was not palpable until shortly before death, when it was felt two fingers below the free border of the ribs. Petechiæ were present. The sternum was tender. Urine examination showed a specific gravity of 1016 to 1028, a trace of albumin, and occasional erythrocytes. Quantities of urine varied from 1500 to 2300 c.c. Blood-examination showed leukocytes, 9200; polymorphonuclears, 61 per cent.; later examination showed leukocytes, 7500; polymorphonuclears, 59 per cent.; hemoglobin, 65 per cent. The temperature was often up to 101° at first, and later 100° (except for rises due to an infection of the maxillary antrum and due to an acute otitis media). Death appeared to be due to embolism. Postmortem examination showed bacteria-free lesions of the aortic and mitral valves. The spleen weighed 420 grams (14 ounces), contained infarctions, and the Malpighian bodies were prominent.

Summary. Pigmentation; renal phenomena; embolism. This is one of the cases in which the patient passed large amounts of urine of high specific gravity.

CASE XI.—Period of observation from December 26, 1911, to January 30, 1912. The patient had previously been in the hospital from March 18 to April 15, 1911. Three blood-cultures were taken, with negative results. On the first admission there was cough and palpitation. Petechiæ were present. Temperature 101°, later 100°. Two days before the date of the second admission there was pain in the right forearm, due to embolism of the brachial artery just before its bifurcation. Examination of the heart revealed insufficiency of the aortic and mitral valves. Spleen was not palpable. Petechiæ were present. The sternum was tender. The urine varied in amount from 900 to 1300 c.c., contained albumin and casts, but no erythrocytes. Blood examination showed leuko-

cytes, 11,000; polymorphonuclears, 71 per cent. There is no record of a hemoglobin estimation, but the patient looked anemic. The temperature was at first 102°, later 101°. Death was due to cardiac insufficiency and anemia. At the postmortem examination there was found a bacteria-free healed lesion of the mitral valve and the chordæ tendineæ. The spleen weighed 135 grams (4½ ounces); there were infarctions present; Malpighian bodies were prominent.

Summary. Endocarditic phenomena and anemia.

CASE XII.—Period of observation from December 28, 1911, to December 31, 1911. One blood-culture was taken, with negative result. The patient had previously been in the hospital from March 24, 1905, to April 11, 1905, and from April 20, 1909, to May 1, 1909. There was a previous history of acute rheumatism. During the first two admissions he was supposed to be suffering from chronic endocarditis and rheumatism. At the time of the last admission he had been sick for four weeks, complaining of dyspnea, cough, cardiac palpitation, night sweats, and chilly sensations; he was very pale. There was marked sternal tenderness. The temperature never rose over 101°. The quantity of urine was at first 2700 c.c., and later dropped to 800 c.c. The urine showed a specific gravity of 1025 to 1028, later 1011. Blood-examination showed leukocytes, 10,000; polymorphonuclears, 78 per cent.; hemoglobin, 53 per cent. The patient died of cardiac insufficiency (and secondary renal insufficiency). Postmortem examination showed slight lesions of the aortic valve and marked lesions of the mitral valve, both bacteria-free. The spleen weighed 540 grams (18 ounces); there were infarctions present.

Summary. Moderately marked anemia; renal phenomena; marked splenic enlargement.

CASE XIII.—Period of observation from January 10, 1912, to March 21, 1913. The patient had been at the hospital from January 10, 1912, to March 5, 1912. There were four blood cultures, with negative results. On the first admission to the hospital the patient was suffering from chronic endocarditis, with pulmonary infarctions and a cerebral hemorrhage (as proved by the bloody character of the lumbar puncture fluid, which was obtained at the time). When admitted on January 10, 1912, he gave a history of having had rheumatism eight years before, and since that time frequent attacks of pain about the heart and shortness of breath and also pains in the extremities. Two weeks before admission he was taken sick with a severe pulmonary hemorrhage; he was also suffering from pains in the region of the heart and the left shoulder-joint, and marked weakness. He developed a brown color of the face under observation. There was sternal tenderness present. The cardiac examination revealed a mitral insufficiency and stenosis and aortic insufficiency. He had repeated attacks of purpura. Tender nodes occurred in November, 1912, and the patient stated that he had had them

already three years before. The urine varied in amount from 1700 to 2000 c.c.; the specific gravity was as high as 1030; there were hyaline casts present. During the period of observation there were several attacks of hematuria. Toward the latter part of the disease no erythrocytes were found. There were two attacks of cerebral embolism. The temperature was usually around 99°, except when embolic phenomena or pulmonary infarctions developed. The patient died of cardiac insufficiency. Postmortem examination showed old, bacteria-free, fibrous lesions of the aortic valve and ulcerative and fibrous lesions of the mitral valve, also bacteria-free. The spleen weighed 240 grams (8 ounces) and was scarred from infarctions. The bone-marrow of the tibia was fatty (that of the femur could not be obtained).

Summary. Endocarditic symptoms (embolisms, purpura); pigmentation; renal phenomena; anemia. Special note is to be made in this case of the excretion of large quantities of urine of high specific gravity (the urine contained few or no formed elements when a large amount of concentrated urine was being passed).

CASE XIV.—Period of observation from February 1, 1913, until the present time, the patient being alive and in little worse condition than when first seen. There were five blood-cultures made, all with negative results. The main features of this case were pigmentation of the face and exquisite tenderness of the lower sternum. The spleen was palpable at one time, and petechiæ were present in the conjunctivæ during the early part of the observation. The patient is in the hospital at the present time suffering from mitral insufficiency, with attacks of decompensation and acute bronchitis.

CASE XV.—Period of observation from September 4, 1911, until the present time, the patient still being alive. One blood-culture was taken, with negative result. This patient suffering from insufficiency of the aortic and mitral valves. He showed marked pigmentation of the face and marked sternal tenderness. The spleen was palpable. He passed large quantities of urine, as high as 2350 c.c. The specific gravity of the urine varied from 1018 to 1027; there was a faint trace of albumin, and erythrocytes were found from time to time. The blood-examination showed leukocytes, 8800; polymorphonuclears, 48 per cent.

CASE XVI.—Period of observation from June 4, 1912, until the present time, the patient being still alive. Two blood cultures were made, with negative results. The patient gave a previous history of rheumatism. Two days before admission to the hospital he was taken sick with dyspnea and cardiac palpitation and pain. Face was markedly pigmented, and there was marked sternal tenderness. Petechiæ were found, and there were evidences of mitral insufficiency. He was becoming progressively more pale, and had lost weight. He was passing from 2800 to 2900 c.c. of

urine; specific gravity, 1008 to 1020; some albumin, hyaline and granular casts, and erythrocytes. Blood count showed leukocytes, 10,000; polymorphonuclears, 65 per cent.; hemoglobin, 50 per cent. The temperature ran from 101° to 102°, and once was 103°.

These last three cases appear to the writer to belong with great certainty, to the group under discussion. Cases XV and XVI are both working at the present time; Case XIV is up and about and is staying in the hospital because of the repeated attacks of bronchitis and asthma. These cases are identical with others that were picked out as clinically belonging in the group, and in which the diagnosis was confirmed by postmortem examination.

CASE XVII.—Period of observation from August 22, 1912. to August 30, 1912. There was one blood-culture, with negative result. There was a previous history of rheumatism. Five weeks before admission to the hospital the patient complained of headache, fever, and chilly sensations. Examinations of the heart revealed insufficiency of the aortic and mitral valves. The patient appeared anemic. Petechiæ were present, and also marked tenderness of the sternum. Urine examination was practically negative. Blood-examination showed leukocytes, 12,000; polymorphonuclears, 76 per cent. The spleen was palpable two fingers below the free border. The temperature never rose above 100.6°. Death was apparently due to embolisms. Postmortem examination showed bacteria-free old lesions of the aortic and mitral valves. The spleen weighed 540 grams (18 ounces); there was marked hyperplasia of the Malpighian bodies; old infarctions were also present. The bone-marrow of the tibia was found to be red in color and microscopically showed changes found in bone-marrow regeneration.

Summary. Embolic phenomena; marked splenic enlargement; regeneration of the bone-marrow in the femur.

CASE XVIII.—This case will not be discussed in detail at the present time. It is the case mentioned above which was suspected of belonging in the group in which there was not sufficient evidence at the postmortem examination to corroborate the clinical diagnosis. It will be described in detail at another time.

CASE XIX.—Period of observation from September 16 to the present time, the patient being still alive. One blood-culture was taken, with negative result. This case is only suspicious and cannot be considered to surely be a case in the group. Three years before admission the patient was suffering from dyspnea and palpitation. There was marked brown pigmentation of the face. There was present a stenosis and insufficiency of the mitral valve and insufficiency of the aortic valve. Spleen was palpable. The sternum was distinctly tender. Quantities of urine varied from 700 to 950 c.c.; specific gravity ranged from 1010 to 1026; there was a faint trace of albumin, some leukocytes, and a few erythrocytes. Blood-count showed leukocytes, 7200; polymorphonuclears, 63 per cent.;

erythrocytes, 5,792,000; hemoglobin, 60 per cent. The temperature was practically normal.

CASE XX.—Period of observation from September 17, 1912, to October 19, 1912. One blood-culture was made, with negative result. The patient was taken sick, one week before admission, with dyspnea, pain the chest, cough, with bloody expectoration, and swelling of the feet. He stated that he had had lesions that corresponded to the tender cutaneous nodules of subacute bacterial endocarditis on three fingers of the left hand three years before admission. The heart presented evidences of mitral stenosis and insufficiency and aortic insufficiency. The spleen was palpable. The patient looked anemic. The sternum was markedly tender. On September 13 the patient developed tender nodules on the thumb of the left hand, and he had had one on the right hand two weeks before. The quantity of urine passed was as high as 2400 c.c. a day; specific gravity varied from 1012 to 1016; erythrocytes were present, also granular and waxy casts. Blood-count showed leukocytes, 13,400; polymorphonuclears, 58 per cent. There was no record of any hemoglobin estimation, but the patient was evidently anemic. The temperature was up to 102° on September 8; after that it was usually around 99° or 100° , with occasional rises to 100.5° . The patient died of uremia. At the postmortem examination there was found a bacteria-free lesion of the aortic valve, slight in extent, and a more marked lesion of the mitral valve. The spleen weighed 450 grams (15 ounces); Malpighian bodies were prominent.

Summary. Occurrence of tender nodules in the bacteria-free period of the disease; anemia; nephritic condition.

CASE XXI.—Period of observation from October 3, 1912, to December 6, 1912. Three blood-cultures were made, with negative results. This was a case which was taken by a number of observers to be one of Banti's disease. The patient, who was aged sixteen years, suffered for four months before admission from epistaxis, weakness, dyspnea, palpitation, swelling of the feet, and increasing pallor. Examination of the heart revealed mitral insufficiency. The spleen was large, being felt four fingers' breadth below the free border. Petechiæ developed during the course of the disease. The color of the face was pale, with a café-au-lait tint. The urine was grossly hemorrhagic from time to time. The specific gravity ranged from 1012 to 1016, and once was 1026. The quantity was from 450 to 1950 c.c. It usually contained erythrocytes and leukocytes, and albumin in fair quantity. Blood examination showed erythrocytes, 2,550,000; hemoglobin, 26 per cent., later 20 per cent.; leukocytes, 6200; polymorphonuclears, 62 per cent.; and later there were, leukocytes 5200, and polymorphonuclears 56 per cent. The temperature at first rose to 103° , later it was only 101° . The patient developed edema of the lower eyelids, vomited repeatedly, and died

in a profoundly uremic condition. At the postmortem examination there were found lesions of the mitral valve and chordæ tendineæ. The spleen weighed 510 grams (17 ounces); the Malpighian bodies were prominent. The cultures made postmortem from the spleen and blood showed an organism corresponding to the coccus generally found in these cases of endocarditis. Spreads made from the lesions in the heart showed absolutely no organisms. It is probable that in this case we are dealing with a case in which the lesions had become bacteria-free or nearly so only a short time before the patient came under observation. The cocci found in the spleen and blood at the time of the postmortem examination may have been thrown out from a few cocci left in some part of the vegetations and from some organ in the body where they had remained in latent condition and had then multiplied after or shortly before death. The fact that no cocci could be found in the vegetations is quite definite proof that the patient was becoming free from the bacterial infection because, as a rule, in all cases in which cocci are found in the blood during life or in postmortem examination the vegetations are full of cocci.

Summary. Marked splenic enlargement; marked renal phenomena; severe anemia; some pigmentation of the face developing under observation.

CASE XXII.—Period of observation from December 3, 1912, to December 11, 1912. Only one blood-culture was taken in this case, and in that a typical pneumococcus was found. The case, nevertheless, belongs in the group of cases which are undergoing spontaneous healing, for reasons which will be given when the postmortem findings are discussed. This patient, who was aged fifteen years, stated that she had had, for five years, frequent attacks of cardiac palpitation and dyspnea. The feet were swollen on frequent occasions. Three weeks before admission she was suddenly seized with cardiac palpitation and weakness, and took to bed. She suffered from cough and expectoration, and these symptoms continued until the time of admission to the hospital. For the last eight or nine days before admission she had been jaundiced. Examination of the heart revealed the presence of mitral stenosis and insufficiency and aortic insufficiency. The spleen was palpable and petechiæ were present. The quantities of urine were 500 to 600 c.c.; specific gravity, 1020 to 1022; hyaline and granular casts, and erythrocytes were present; bile was easily demonstrable. Blood-examination showed hemoglobin 48 per cent. The temperature remained around 100° until December 5, when it rose to 105°; on the following days it was up to 103°. This rise of temperature was due to a lobar pneumonia, of which the patient died. At the postmortem examination there was found a bacteria-free lesion of the auricle and mitral valve. The spleen was twice the normal size, and there were old infarctions present. The kidneys showed typical embolic

glomerular lesions, all in the healed state. Because the lesions in the heart were rather old and bacteria-free, and because the embolic lesions in the kidney were all completely healed, and there was practically no temperature up to the time that the pneumonia developed, the writer is of the opinion that the presence of pneumococci in the blood was due to a lobar pneumonia developing in a person who was in the bacteria-free stage of subacute bacterial endocarditis.

Summary. Marked anemia; renal phenomena; terminal pneumonia.

THE NOGUCHI LUTETIN REACTION IN SYPHILIS.¹

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PERHAPS there is no disease which is characterized by a greater diversity of pathological lesions or is more protean in its manifestations than syphilis. With a clear history of infection and the existence of tell-tale lesions a definite diagnosis may be made without hesitation. A clear history, however, often cannot be elicited, nor are unmistakable lesions always present. The vague symptoms and signs which indicate the insidious development of internal lesions or the early stages of parasymphilitic conditions may suggest syphilis to the trained syphilographer, but in only too many instances a definite diagnosis is attended with insurmountable difficulties for the average practitioner.

In recent years the laboratory has come to the aid of the clinician in diagnosing these obscure cases. The Wassermann test is a valuable addition to our armamentarium, but one that is infallible by no means. Certain cases of frank syphilis may never give a positive reaction; the sera of those suffering with leprosy, malaria, yaws, etc., may react positively; treatment may render negative the test despite the persistence of active manifestations; and, finally, in view of the technical knowledge required to properly perform the test, the results are not reliable unless the tests have been made by a trained serologist.

The examination of fresh preparations from active lesions may reveal spirochetes that are diagnostic, but this method is applicable only to lesions which by their objective characteristics alone should suggest syphilis to one who knows the disease. Furthermore, various mouth spirochetes may be confused with the specific treponema of syphilis unless the microscopist be an expert.

As neither clinical nor present laboratory methods are devoid

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of possibilities of error, it is obvious that a means of diagnosis that is specific for syphilis, reasonably delicate, easy of application and interpretation, and innocuous as regards the patient, is still needed. The Noguchi luetin test gives promise of fulfilling this need in certain cases.

Stimulated by von Pirquet's demonstration of the cutaneous reaction in tuberculosis, numerous investigators attempted to obtain a similar reaction in syphilis by applying extracts of syphilitic tissues to the skin of luetic individuals. Their results were contradictory. Noguchi² states that Neisser and Bruck showed that a reaction similar to that obtained with the luetic extracts could be induced, also, with concentrated extract of normal liver. This peculiar susceptibility of the skin of chronic syphilitics to any form of chemical irritation was designated by Neisser as the state of "Umstimmung." Despite his discouraging results, Neisser expressed the hope that the reaction might be improved by employing an extract of the specific organism of syphilis, free from organic constituents. Improvement along these lines was made possible subsequently by the successful cultivation of *Treponema pallidum* in pure cultures by Noguchi.³

PREPARATION OF LUTIN. Noguchi describes the preparation of his luetin as follows: "Pure cultures of several strains of the pallidum are allowed to grow for periods of six, twelve, twenty-four, and fifty days at 37° C., under anaërobic conditions. One set is cultivated in ascitic fluid containing a piece of sterile placenta, and the other in ascitic fluid agar also containing placenta. The lower portion of each solid culture in which a dense growth has occurred is cut out and the tissue removed. The agar columns which contain innumerable spirochetæ are then carefully ground in a sterile mortar. The resulting thick paste is gradually diluted by adding, little by little, the fluid culture which also contains an enormous mass of the pure organisms.

"The dilution is continued until the emulsion becomes perfectly liquid. The preparation is next heated to 60° C. for thirty minutes in a water-bath and then 0.5 per cent. tricresol is added. When examined under the dark-field microscope, numerous dead pallida per field may be seen. Cultures made from this suspension remain sterile and with it no infection can be produced in the testicles of rabbits. The suspension is kept in a refrigerator when not in use.

"In order to ascertain whether the reaction with this suspension might not be due to the introduction of antiseptic culture medium alone, it is necessary to prepare a similar emulsion, with uninoculated media, to be used for control purposes."

² A Cutaneous Reaction in Syphilis, Jour. Exper. Med., 1911, xiv, 557.

³ Experimental Research in Syphilis, with Special Reference to *Spirochæta pallida* (*Treponema pallidum*), Jour. Amer. Med. Assoc., 1912, lviii, 1163.

APPLYING THE TEST. Several months ago the writer received from Dr. Noguchi sufficient luetin to apply the test to a series of cases. All my cases were from the out-patient venereal service of the Post Hospital, Fort Leavenworth, Kansas, and the United States Penitentiary, Leavenworth, Kansas. The test was applied to seventy-five persons, seventy of whom at the time were or had been infected with syphilis, while the remaining five individuals were used as normal controls.

The technique recommended by Noguchi was carefully followed in applying the tests. The sterile vials of luetin and control emulsion were thoroughly shaken and the desired amounts of each were then removed from the containers with sterile pipettes and diluted with an equal amount of sterile salt solution. The arms, at the proposed site of inoculation, were thoroughly cleansed with alcoholic sublimate solution. New graduated tuberculin syringes fitted with very fine needles were used in making the inoculations. The syringes were sterilized by boiling, labelled so that no possibility of using the control syringe for luetin emulsion, or *vice versa*, existed, and separate needles were used for each case. The luetin emulsion (0.07 c.c., accurately measured by the graduations on the syringe) was injected intradermically into the skin of the left arm and the control emulsion, in like manner and quantity, was injected into the skin of the right arm. Care was exercised that the inoculations were made very superficially, so as just to raise the epidermis.

In forty-eight cases the reactions were noted daily for a period of ten days, and, subsequently, at periods of two to four days. In the remaining cases the reactions were examined every three to five days. All cases were under observation for from three to five weeks and a note was made of the changes in the individual reactions at each examination.

CHARACTER OF REACTIONS. It was noted that injections of both luetin and control emulsions produced a circumscribed, elevated, blanched swelling about 4 mm. in diameter, similar in appearance to the lesion produced by the bite of an insect in certain persons.

This local swelling entirely disappears in a half hour or so. In positive cases, after twenty-four hours, there is usually more or less inflammatory reaction at the luetin site, manifested by a distinct, circumscribed, indurated, bright red papule. This papule may be surrounded by a hyperemic areola. A reaction may or may not occur at the site of the control injection. When present the control lesion does not exhibit the same degree of induration as the luetin lesion, but otherwise it may appear identical.

At the end of forty-eight hours the luetin papule has become larger, more indurated, and may be surrounded by an inflammatory areola, from which radiate lines of telangiectasis. This marked

inflammatory reaction occurs more commonly between the fourth and seventh days. The control papule, when present, begins to fade in twenty-four hours, and has usually disappeared within three



FIG. 1.—Became infected in October, 1911. No active lesions at present. Wassermann positive in June, 1912. The left arm shows a distinct pustular luetin reaction with inflammatory areola, while the right arm shows no trace of the control injection. Photograph taken on the tenth day.



FIG. 2.—Infected in 1908. Treated with mercury and salvarsan. No active manifestations at present. Wassermann negative. Left arm shows a distinct papular luetin reaction. Photograph taken on fifth day.

days. In a few cases, however, beside those evidencing the state of "Umstimmung," more or less discoloration remains at the control site for several days. For this reason I believe that one is

not justified in making a final reading of the reaction before the seventh day. Control lesions which are not due to "Umstimmung" will have disappeared by that time, while positive luetin reactions will still persist, being, as a rule, more marked than on the second or third days. From the second to the sixth or seventh days the reaction becomes progressively intensive. The centre of the papule becomes boggy and deep purplish red in color, and the lesion may be surrounded by an erythematous blush.

As a rule no systemic reaction accompanies the local lesion, but in a few cases there may be complaint of considerable itching and some soreness of the arm. In only one of my cases, was there an appreciable systemic reaction. This patient reported the second day following inoculation with a temperature of 102° F., and complained of brow-ache, malaise, and "soreness all over." His symptoms disappeared entirely in twenty-four hours without treatment.



FIG. 3.—Infected in 1909. Treated with mercury for eighteen months during 1909-10. No active lesions at present. Wassermann strongly positive. The left arm shows the appearance of a luetin pustule on the fifth day.

The papular form of reaction begins to fade about the end of the first week, coincidentally with which desquamation of the epidermis over the papule, and in the more intense reactions for an area around it, occurs. The induration remains for several days after the inflammatory signs have disappeared and its subsidence is followed, in turn, by an area of bluish discoloration which persists in many cases for two or three weeks.

The above description is a brief *resume* of the stages observed in the average papular reaction. In certain cases the lesion be-

comes pustular, usually on the fifth day, followed by rupture of the pustule, as a rule on the seventh day, and crust formation. These pustular reactions seem to bear a rather definite relation to the treatment instituted—a phenomenon that will be discussed later.

A third type of reaction, the torpid form, was observed in two of the cases. In these cases the initial reaction subsided within three or four days, but lighted up again ten days and fifteen days respectively after inoculation and then went through the various stages of the typical luetin papule in one case and pustule in the other.

For purposes of analysis the cases to which the tests were applied may be divided into four series: Series "A" embodies cases exhibiting active secondary manifestations; Series "B" consists of cases showing tertiary lesions; Series "C" covers cases of syphilis with clear histories of infection, but, at the time, latent or cured; Series "D" embraces normal individuals, used as controls. A tabulation of these cases follows:

TABULATION OF LUTIN RESULTS.

SERIES A—SECONDARY SYPHILIS.

CASE 1.—Mucous patches in mouth and general adenopathy. Inunctions of mercury for five months early in 1911. Mercury internally for two months a year ago. Wassermann negative. Positive pustular luetin reaction.

CASE 2.—Mucous patch on tonsil and general adenopathy. Mercury and potassium iodide intermittently for four months in 1912. Wassermann negative. Positive pustular luetin reaction.

CASE 3.—Mucous patches in mouth. Treated with mercury for eleven months following infection. Wassermann positive. Luetin reaction positive papular ("Umstimmung").

CASE 4.—Mucous patches in mouth, and condylomata, general adenopathy, and osteocopic pains. Potassium iodide for three weeks followed by twelve injections of sodium cacodylate. Wassermann positive. Weak papular luetin reaction.

CASE 5.—Cachexia, alopecia, and osteoscopic pains. Salvarsan intravenously in May and November, 1912. Protoiodide by mouth during the past month. Wassermann positive. Luetin reaction negative.

CASE 6.—Mucous patches in mouth. Protoiodide by mouth for six months followed by two intravenous treatments with salvarsan and mercury by mouth during the last five weeks. Wassermann positive. Weak positive papular luetin reaction.

CASE 7.—Mucous patches under tongue. Inunctions of mercury for three weeks in May, 1912, followed by intramuscular injection

of salvarsan. Wassermann weakly positive. Positive pustular luetin reaction.

CASE 8.—Mucous patches and infiltration of fauces. Salvarsan intravenously in September, 1912. Wassermann weakly positive. Positive papular luetin reaction appearing on tenth day (torpid form).

CASE 9.—Mucous patches in throat. Salvarsan intravenously in March, 1912, followed inunctions of mercury for four weeks. Wassermann negative. Luetin reaction negative.

CASE 10.—Maculopapular eruption, adenopathy, and sore throat. Intravenous injection of salvarsan three days before tests were applied. Wassermann positive. Positive papular luetin reaction.

CASE 11.—Mucous patches in mouth and occasional osteo-copic pains. Mercury by mouth and inunction for two months early in 1911. Salvarsan intravenously in June, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 12.—Mucous patches in mouth and general adenopathy. Salvarsan intravenously a month ago followed by four intramuscular injections of gray oil. Wassermann negative. Luetin reaction negative.

CASE 13.—General macular eruption, mucous patches, and adenopathy. Two intramuscular injections of gray oil followed by neosalvarsan intravenously forty-eight hours before tests were applied. Wassermann positive. Positive pustular reaction at site of luetin injection appearing fifteen days after inoculation. Papule at site of control ("Umstimmung").

SERIES B—TERTIARY SYPHILIS.

CASE 1.—Gummatous ulcers and cicatrices on leg. Primary sore seven years ago. Clear history of secondaries. Mercury and potassium iodide intermittently for past six years. Five injections of sodium cacodylate recently. Wassermann negative. Positive papular luetin reaction.

CASE 2.—Rupial lesions, alopecia, and general adenopathy. Chancre five years ago. Protoiodide and potassium iodide routinely during past two years. Seven injections of sodium cacodylate recently. Wassermann negative. Weak positive papular luetin reaction.

CASE 3.—Rupial lesions. Not certain of date of infection. Protoiodide by mouth during the past month. Twelve injections of sodium cacodylate. Wassermann negative. Weak positive papular luetin reaction.

CASE 4.—Persistent headache worse at night. Clear history of chancre in 1907, followed by secondaries. Intramuscular injections of mercury and potassium iodide by mouth from January

to April, 1908. "Cook's Remedy" during May, 1908. Mercury and potassium iodide during the entire year 1909. Wassermann negative seven consecutive times during the past seven months. Luetin reaction negative.

CASE 5.—Syphilitic orchitis. Denies infection or history of secondaries. Wassermann strongly positive before treatment—now negative. Salvarsan intravenously two weeks before application of tests followed by injection of gray oil. Wassermann negative. Positive pustular luetin reaction.

SERIES C—CONTROLLED SYPHILIS.

CASE 1.—Infected in September, 1911, clear history, no active lesions at present. Salvarsan intramuscularly in February, 1912, preceded and followed by inunctions of mercury. Wassermann strongly positive before treatment and negative at monthly intervals since that time. Positive papular luetin reaction.

CASE 2.—Infected in 1910, clear history, no active lesions at present. Mercury by mouth for two months following appearance of secondaries, salvarsan intramuscularly in 1911, and mixed treatment during the period August to October, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 3.—Infected in 1894. No active lesions at present. Has been treated intermittently with mercury during past eighteen years. Wassermann negative. Strong positive pustular luetin reaction.

CASE 4.—Infected in May, 1911. No symptoms at present. No definite history of treatment can be procured. Wassermann negative. Positive papular luetin reaction.

CASE 5.—Infected a year ago. No active lesions. Mercury by mouth for nine months following infection. Wassermann weakly positive. Positive pustular luetin reaction.

CASE 6.—Infected in October, 1911. No symptoms at present. Protoiodide for nine months followed by potassium iodide for past three months. Wassermann negative. Positive pustular luetin reaction.

CASE 7.—Infected a year ago. No lesions at present. Treated with protoiodide for three months followed by twelve injections of sodium cacodylate. Wassermann strongly positive. Weak positive papular luetin reaction.

CASE 8.—Infected in June, 1909. No lesions at present. Received inunctions of mercury for one month in 1909 followed by a specific mixture (nature not elicited) for a year. No treatment during 1911–12. Wassermann negative. Weak positive papular luetin reaction.

CASE 9.—Infected in 1907. No active lesions at present. Mercury by mouth and inunction for one year. No treatment during

past four years. Wassermann weakly positive. Weak positive papule at both luetin and control sites ("Umstimmung").

CASE 10.—Infected in 1911. No symptoms at present. Wassermann strongly positive before treatment. Salvarsan intravenously in May, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 11.—Infected in 1904. No active lesions at present. Mercury during the entire year 1905 and potassium iodide during June, 1912. Wassermann positive in April, 1912, now negative. Distinct positive papular luetin reaction.

CASE 12.—Infected in 1902. No active lesions now. Wassermann positive on five occasions during the period April to October, 1911. Two intravenous and one intramuscular administrations of salvarsan in March, June, and October, 1911, respectively. Wassermann now weakly positive. Luetin reaction negative.

CASE 13.—Infected in June, 1912. No lesions at present. Wassermann positive before treatment. Salvarsan intravenously on November 4 and 23, 1912, followed by four injections of gray oil. Wassermann reaction still positive. Luetin reaction negative.

CASE 14.—Infected in October, 1911. No symptoms at present. Wassermann positive before treatment. Inunctions of mercury during November, 1911. Protoiodide by mouth during February, 1912, followed by salvarsan. Wassermann negative. Positive papular luetin reaction.

CASE 15.—Infected in December, 1911. No lesions at present. Wassermann weakly positive before treatment. Intramuscular injection of salvarsan, January 28, 1912. Wassermann negative. Weak positive papular luetin reaction.

CASE 16.—Infected in July, 1912. No manifestations at present. Inunctions of mercury during the past six months. Wassermann weakly positive. Weak papular luetin reaction.

CASE 17.—Infected in October, 1910. No active lesions at present. Wassermann reaction strongly positive on several (five) occasions before and after treatment. Mercury during March, 1911, followed by intravenous treatment with salvarsan. Salvarsan intramuscularly on September 7, 1911. Wassermann now negative. Distinct papular reaction at sites of injection of both luetin and control ("Umstimmung").

CASE 18.—Infected in May, 1909. No active manifestations. Mercury for one month in 1909. Patient denies further treatment. Wassermann negative. Weak positive papular luetin reaction. (Constitutional manifestations followed the injection of luetin in this case. Patient complained of "soreness all over," and brow-ache forty-eight hours after inoculation. Temperature, 102° F. All symptoms disappeared, without treatment, in twenty-four hours.)

CASE 19.—Infected in August, 1911. Salvarsan intravenously in September, 1911, December, 1911, and April, 1912. Wassermann negative. Positive pustular luetin reaction (state of "Umstimmung" present for five days).

CASE 20.—Infected for eighteen months. No active lesions. Mercury by mouth for one month during 1912. Wassermann negative. Positive papular luetin reaction ("Umstimmung").

CASE 21.—Infected August 25, 1911. No symptoms at present. Wassermann positive before treatment. Inunctions of mercury for three weeks in September, 1911; salvarsan intravenously in October, 1911; intramuscular injections of mercury in October, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 22.—Infected in January, 1902. No active manifestations. Wassermann positive before treatment. Mercury for two years, 1901-02. Salvarsan intravenously September 19, 1911. Wassermann negative. Positive papular luetin reaction.

CASE 23.—Infected in July, 1911. No active lesions at present. Mercury for three months in 1911. Wassermann negative. Positive papular luetin reaction.

CASE 24.—Infected in December, 1909. No active lesions now. Wassermann positive early in 1911. Salvarsan intravenously in March, and again in April, 1911. Wassermann negative. Positive papular luetin reaction.

CASE 25.—Infected in September, 1911. No manifestations at present. Wassermann strongly positive before treatment. Salvarsan intramuscularly November 27, 1911. Wassermann weakly positive. Positive pustular luetin reaction.

CASE 26.—Infected in February, 1909. Clear history of typical secondaries. Wassermann positive on five occasions during the period July to October, 1911. Salvarsan intravenously in July, 1911. Wassermann negative. Weak positive papular luetin reaction.

CASE 27.—Infected in 1909. No active lesions at present. Protoiodide by mouth for eighteen months during 1910-11. Wassermann strongly positive. Positive pustular luetin reaction.

CASE 28.—Infected in December, 1911. No active manifestations now. Wassermann negative at monthly intervals for six months following treatment, though positive prior to treatment. Salvarsan intramuscularly February 3, 1912. Patient gained twenty-five pounds after treatment. Wassermann still negative. Luetin reaction negative.

CASE 29.—Infected in December, 1911. No active lesions since treatment. Positive Wassermann before treatment. Salvarsan intramuscularly February 3, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 30.—Infected in February, 1912. No active lesions at present. Wassermann positive before treatment and persisted after first treatment with salvarsan. Salvarsan intravenously in

May and August, 1912. Wassermann negative after second treatment but now positive. Weak positive papular luetin reaction.

CASE 31.—Infected in 1902. No manifestations at present. Four consecutive positive Wassermann tests in the period October, 1911, to February, 1912. Salvarsan intravenously in September, 1911. Wassermann negative. Weak positive papular luetin reaction.

CASE 32.—Infected in November, 1911. No symptoms at present. Wassermann positive before treatment. Salvarsan intravenously February 3, 1912. Wassermann negative. Positive pustular luetin reaction.

CASE 33.—Infected in November, 1911. No lesions now. Inunctions of mercury followed by salvarsan intravenously in March, 1912. Wassermann positive before treatment with salvarsan, now negative. Weak positive papular luetin reaction.

CASE 34.—Infected in October, 1911. No active lesions at present. Wassermann positive in June, 1912. No record of treatment and soldier denies having been treated elsewhere. Wassermann now negative. Positive pustular luetin reaction. (Distinct pustule appeared at site of control injection sixteen days after inoculation. Its development was coincident with the beginning disappearance of the luetin pustule. Delayed "Umstimmung?")

CASE 35.—Infected in 1901. No active manifestations at present. Wassermann strongly positive in April, 1911. Salvarsan intravenously April 18, 1911. Wassermann subsequently and now negative. Weak positive papular luetin reaction.

CASE 36.—Infected in February, 1911. No symptoms at present. Two intravenous and one intramuscular administrations of salvarsan during April and May, 1911. Mercury and potassium iodide during July, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 37.—Infected in July, 1912. Clear history and positive Wassermann before treatment. Inunctions of mercury for one week followed by salvarsan intravenously on September 18, 1912. Wassermann negative. Positive papular luetin reaction.

CASE 38.—Infected in December, 1910. No manifestations at present. Protoiodide by mouth for three months followed by salvarsan intramuscularly. Wassermann weakly positive. Positive papular luetin reaction.

CASE 39.—Infected in 1905. No active lesions. Wassermann positive a year ago. Inunctions of mercury for two months followed by salvarsan intramuscularly on May 22, 1912. Wassermann negative. Weak positive papular luetin reaction.

CASE 40.—Infected in July, 1912. Typical secondaries in September. No lesions at present. Salvarsan intravenously three times during the past three months. Wassermann negative. Positive papular luetin reaction.

CASE 41.—Infected October 4, 1911. Wassermann positive November 5, 1911. Inunctions of mercury from November 3, 1911 to January 26, 1912. Salvarsan intramuscularly November 12, 1911. No lesions at present. Wassermann negative. Positive papular luetin reaction.

CASE 42.—Infected in July, 1909. Wassermann positive in July and November, 1911. Salvarsan intravenously July 2, 1911, followed by inunctions for three months and mercury by mouth for one month. No active manifestations now. Wassermann negative. Weak positive papular luetin reaction.

CASE 43.—Infected in February, 1910. Wassermann strongly positive in June, 1911. Intramuscular injections of mercury May to October, 1910. Salvarsan intravenously June 26, 1911. No lesions now. Wassermann negative. Positive papular luetin reaction.

CASE 44.—Infected in April, 1912. Wassermann weakly positive in May, 1912. Salvarsan intravenously May 23, 1912. No symptoms during past six months. Wassermann negative. Luetin reaction negative.

CASE 45.—Infected in March, 1908. Clear history of secondaries. Treated with mercury from June, 1909, to May, 1910, potassium iodide during July, 1910, salvarsan intravenously March 29, 1911. Wassermann negative. Positive pustular luetin reaction.

CASE 46.—Infected in 1907. Wassermann positive in October, 1912. Treated energetically with mercury for two years, 1907-09. Salvarsan intravenously in October, 1912. Wassermann test has been negative at monthly intervals since treatment with salvarsan. Patient is somewhat anemic, but exhibits no active manifestations. Weak positive papular luetin reaction.

CASE 47.—Infected in 1898. Clear history of secondaries. Wassermann reaction positive before and after treatment in 1911, at Manila, P. I. Salvarsan intravenously, at Manila, P. I., in July, 1911. Wassermann negative at monthly intervals for past four months. No active lesions at present, but patient is anemic and below normal tone. Positive papular luetin reaction.

CASE 48.—Infected in October, 1911. Disease ran a malignant course and was not influenced by mercury. Wassermann strongly positive before treatment with salvarsan. Salvarsan intravenously in March, 1912, followed by inunctions of mercury for three months, and mixed treatment during July, 1912. No active lesions now. Wassermann negative. Strong positive papular luetin reaction.

CASE 49.—Infected in October, 1911. Wassermann positive in November, 1911. Chancre excised, salvarsan administered intramuscularly, followed by inunctions of mercury for two months. Patient gained weight, has remained without symptoms, and Wassermann has been negative at monthly intervals to date. Luetin reaction negative.

CASE 50.—Infected in December, 1911. Wassermann positive January 15, 1912. Salvarsan intravenously January 16 and 24, 1912. No active lesions during 1912. Wassermann negative. Positive papular luetin reaction.

CASE 51.—Infected in June, 1911. Typical secondaries—mucous patches, maculopapular eruption, alopecia, and adenopathy. Wassermann tests at Fort Leavenworth and Washington laboratories repeatedly negative before treatment. Salvarsan intravenously November 4 and November 27, 1912, followed by two injections of gray oil. No active lesions at present. Wassermann negative. Weak positive papular luetin reaction (“Umstimung”).

CASE 52.—Infected in June, 1910. Wassermann positive in July, 1911. Salvarsan intravenously in July, 1911, followed by mixed treatment for one month. Protoiodide by mouth during December, 1911. No active manifestations since that time. Wassermann negative. Luetin reaction negative.

SERIES D—CONTROL CASES.

CASE 1.—Married, non-commissioned officer with healthy children. Denies venereal history. Diphtheria a year ago. Throat culture positive for K-L bacillus. Wassermann at that time negative. No antisyphilitic treatment. Wassermann negative. Luetin test negative.

CASE 2.—Robust young soldier. Denies venereal disease. Careful physical examination fails to reveal signs of acquired syphilis or any of the stigmas of congenital lues. These findings concurred in by one of the best syphilographers in the army. Wassermann negative. Typical strong positive papular luetin reaction. Family history shows one grandparent to have had tabs.

CASE 3.—Normal young adult male (laboratory assistant). No history of venereal disease. Wassermann and luetin tests negative.

CASE 4.—Young soldier. Denies venereal disease. No clinical evidence of congenital or acquired lues. Wassermann negative. Luetin test negative.

CASE 5.—Young soldier. Has three typical chancroids which appeared five days after intercourse. History of a single sore, similar to those he now exhibits, three years ago. Treated locally by a druggist and healed in a week or so. No specific treatment. No clinical evidences of syphilis. Wassermann negative. Luetin test negative.

ANALYSIS OF RESULTS. By reference to the above summary it will be observed that the luetin test was applied to 13 cases of secondary treated syphilis; 5 cases which exhibited tertiary lesions;

52 cases of syphilis in the stage of latency or cure; and 5 individuals presumably free from syphilis.

The percentage of positive reactions among the treated cases of secondary lues was 77 per cent.; of the tertiary cases, 80 per cent. reacted positively; while among the cases which had reached a stage of latency, 88 per cent. gave a positive reaction. Of the 5 apparently normal individuals used as controls, 1 case developed a typical papular reaction. This occurrence is of considerable moment, as the value of the test hinges largely on its specificity. The case in question was that of a perfectly healthy young soldier who denied absolutely the possibility of syphilis. Careful physical examination failed to demonstrate signs of syphilis, and the Wassermann test was negative on three occasions. The family history revealed the fact that the maternal grandmother suffered with an ailment for several years which, from the recital of symptoms, was probably tabes. It has been demonstrated experimentally that the state of allergy or anaphylaxis (upon which the luetin reaction depends) may be transmitted from a sensitized guinea-pig to her offspring and that this transmission can occur only through the female. This raises the very interesting query as to whether a state of allergy, transmitted from a luetic maternal grandmother, might not explain the positive luetin reaction in the case under discussion. Personally, I am inclined to this belief, for, in view of the mass of evidence in favor of the specificity of the test as the result of observations of numerous investigators covering hundreds of cases, it would be presumptuous to contend that the test is not specific because of this one apparently discordant result.

The relative value of the Wassermann and luetin tests is strikingly illustrated in the above series of cases. An opportunity was not offered to apply the luetin test to cases of primary or secondary untreated syphilis, but the work of others seems to show definitely that the reaction rarely occurs in the early stages of the disease. It is in the earlier stages of syphilis that the highest percentage of positive results are obtained with the Wassermann test, while in the later stages the lipotropic substances, upon which a positive reaction depends, are frequently not present in the serum due to fluctuations in the activity of the spirochetæ, induced by treatment or by the production of antibodies which neutralize these lipotropic substances. On the other hand, these fluctuations in the activity of the spirochetæ favor the development of the state of allergy or anaphylaxis, which must be induced before the skin will react to the injection of luetin. In other words, a positive Wassermann test indicates the presence of metabolic substances in the serum, due to present or recent activity of numbers of spirochetæ on the tissues; while a positive luetin reaction is indicative of a state of hypersensitiveness to the specific

proteins of the spirochetæ, induced by a period of cessation of the introduction of these proteins prior to the injection of the luetin.

The results obtained practically with the Wassermann and luetin tests in my series of cases supports the foregoing theoretical assumption. The cases which reacted most intensely to the luetin were, as a rule, those in which the Wassermann test was negative, and *vice versa*.

A casual glance at the brief summaries of the cases outlined above will show the value of the luetin test as a diagnostic measure in the tertiary and latent stages of syphilis, but its greatest value, from my limited experience, appears to be as a means of prognosis. In seventy cases of undoubted syphilis, practically all of whom had been treated, either clinical evidence, a positive Wassermann test, or a positive luetin reaction showed that the syphilitic infection had not been entirely suppressed in all but four cases. It seems reasonable to assume that these latter cases (Cases 28, 44, 49, and 52, Series "C") may be registered as cured.

In view of these results, a provocative injection of salvarsan followed by the application of both Wassermann and luetin tests is suggested as a rational means of determining whether treatment has been sufficiently intensive to effect a cure.

It is a pleasure to thank Dr. Hideyo Noguchi, of the Rockefeller Institute, New York City, for the luetin used in the tests reported herein, and to acknowledge my indebtedness to Major F. M. Hartsock, Medical Corps, United States Army, and Dr. Yohe, of the Federal Penitentiary, Leavenworth, Kansas, for the cases to whom the tests were applied.

BIBLIOGRAPHY.

- Cohen. Noguchi's Cutaneous Luetin Reaction and its Application in Ophthalmology, Arch. Ophth., 1912, xli, 8.
- Orleman-Robinson. The Noguchi Method of Serum Diagnosis of Syphilis; its Practical Value, Med. Record, July 23, 1910.
- Wolfsohn. The Cutaneous Reaction of Syphilis, Bull. Johns Hopkins Hospital, 1912, xxiii, 223.
- Nobl and Fluss. Zur Intrakutanreaktion bei Syphilis, Wien. klin. Woch., 1912, xxv, 475.
- Kämmerer. Diagnostische Intrakutanreaktion mit Spirochätenextrakt, Münch. med. Woch., 1912, lix, 1534.
- Loewenstein. Die Luetinreaktion nach Noguchi bei Augenkrankheiten, Med. Klinik, 1913, ix, 410.
- Rytina. The Luetin Skin Test in the Diagnosis of Syphilis, Med. Record, 1913, lxxxiii, 384.
- Gradwohl. Luetin Test for Syphilis, Med. Record, 1912, lxxxi, No. 21, 973.

DORSAL PERCUSSION IN ENLARGEMENTS OF THE TRACHEOBRONCHIAL GLANDS.

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THIS study represents an attempt to determine the practical diagnostic value of vertebral percussion in that familiar group of tracheobronchial enlargements so frequently met with as sequels of pertussis, measles, and tonsillitis, and as the result of tuberculosis. Secondly, data has been sought whereby differences might be established between the percussion findings in simple adenopathies and in the more extensive neoplastic tumors of the mediastinal space. As a basis of comparison, in the cases under consideration the normal acoustic and tactile characteristics of the percussion zones of the spine were taken as criteria, together with certain acknowledged modifications thereof produced by different thoracic diseases: fibroma, malignant tumor, gumma, and dense fibrosis of the lungs and pleura. Lesions such as these account for physical signs relating not only to the thoracic walls, but also to the thoracic segment of the spine, where more or less definite tonal and topographic changes in the normal percussion zone are apparent.

The dulling effect of tracheobronchial adenopathies upon the thoracic wall has long been an accepted fact, but comparatively few clinicians have championed the procedure of vertebral percussion as a means of investigating this very common and often overlooked condition. One-fourth of all cases of healed pulmonary tuberculosis reveal tracheobronchial adenopathies at autopsy, according to Adami and McCrae.¹ As long as fifteen years ago Fernet² drew attention to the causal relationship between tuberculous bronchial adenitis and bilateral paraspinal dulness, but the dulling of the spine itself under a similar circumstance was not fully appreciated as a clinical finding until the appearance of von Korányi's convincing studies of vertebral percussion, eight years later.³ This despite Ewart's important article on "Dorsal Percussion," published in 1899.⁴ This author, employing instrumental pleximeter percussion, delineated upon the normal spine an isolated relative dulness of the fifth thoracic spine attributable to the "influences due especially to the infratracheal glands," and he also mapped out areas of "visceral dulness" over segments of the spine corresponding to the heart and the liver. As an illustration of the relative frequency of spinal and of mural dulness in tracheo-

¹ Trans. Sixth Internat. Congress for Tuberculosis, 1908, i, 325.

² Bull. de l'Acad. de méd., 1898, xl, 253.

³ Zeitschr. f. klin. Med., 1906, lx, 295.

⁴ Lancet, 1899, ii, 261.

bronchial enlargements it is instructive to note the results obtained by Stoll,⁵ who found the incidence virtually the same (22 per cent. and 23 per cent. respectively) in 175 patients, presumably subjects of bronchoadenopathy. For more recent studies on the diagnosis of this condition and the application of dorsal percussion thereto the reader is referred to articles by Philippi and Schultz,⁶ by Grenet,⁷ and by Zabel.⁸

Honeij's clinical examinations⁹ of 147 patients with questionable and proved phthisis showed that approximately 24 per cent. had enlarged glands at the root of the lung, while still more noteworthy is the same author's uniform demonstration of mediastinal adenopathy in a series of 32 non-tuberculous subjects, classified as "questionable" and as "proved negative" with regard to the diagnosis of pulmonary tuberculosis.

In the healthy adult, gentle finger percussion of the thoracic vertebral processes yields an upper zone of impaired resonance, with appreciable tactile resistance over the first two or three spines, below which there is uniform osteal resonance over the remaining spinous tips. This upper hyporesonant zone has been carefully studied and delineated by Korányi,¹⁰ and although this author's conclusions have not received merited recognition in all quarters, his findings should be obvious to anyone who, careful of technique, studies the subject with an open mind. The relative dullness of the upper thoracic vertebræ is best explained by assuming that these osseous disks are more or less sensitive to the dulling properties of the adjacent cervical segment of the spine. The cervical spine, despite its intimate proximity to the prevertebral air passages and to the esophagus, is anatomically unfitted to generate wholly resonant percussion waves, for such attempts are damped, at least to some degree, by the unyielding, rigid structure of this part of the spine due to its short length, compact components, tense ligamentous attachments, and absence of articulating ribs for the conduction of lateral vibrations. These and the other peculiarities of the thoracic spine in its role as a pleximeter in the production and transmission of percussion waves have been discussed in detail by the writer in an earlier article.¹¹

Ewart¹² calls attention to the clinical utility of mapping out, by pleximetric percussion, an ovoid parasternal area of impaired pulmonary resonance between the levels of the first and the fifth thoracic vertebral spines. This area, termed the "sub-

⁵ Cited by Honeij, v. i.

⁶ Beitr. z. klin. d. Tuberkulose, 1911, xxi, 116.

⁷ Ann. de méd. et chir. infant., 1911, xv, 497.

⁸ Münch. med. Woch., 1912, lix, 2664.

⁹ Jour. Amer. Med. Assoc., 1911, lvii, 958.

¹⁰ Loc. cit.

¹¹ AMER. JOUR. MED. SCI., 1909, cxxxviii, 815.

¹² British Med. Jour., 1912, ii, 966.

resonant interspinous dull patch," in the normal adult extends vertically for a distance of about 110 mm., and has a transverse equatorial diameter of approximately 90 mm., each lateral boundary being equidistant from the midspinal line. Ewart, furthermore, is able to distinguish a normal respiratory variation in the transverse extent of this area, which contracts laterally with deep inspiration and correspondingly expands with expiration, as the volume of the adjacent lungs alternately increases and diminishes. The real value of the "subresonant patch" in the study of tracheobronchial glandular tumors (which lesions can be reasonably expected to alter the characteristic ovoid outline and to restrict the respiratory contour) is still undetermined in the absence of convincing clinical data. Personally, attempts to employ Ewart's area in investigating mediastinal lesions proved of no more conclusive value than the more familiar manner of percussing the dorsal thorax according to conventional technique.

Apropos of the subject of dorsal percussion in general, it may be remarked that a similar technical difficulty would seem to bar the general application of Minerbi's clever, though most delicate, procedure¹³ of delimiting a so-called "aortic and azygos vein zone of dorsal hyporesonance:" a paravertebral area of impaired resonance about 34 cm. long, at the level of the third thoracic spine, and corresponding anatomically to the impingement of the aorta and of the azygos vein upon the mediastinal wall.

INTRATHORACIC FACTORS OF VERTEBRAL PERCUSSION SOUNDS. The exact mechanism whereby intrathoracic lesions, particularly those springing from the mediastinal space, affect the percussion sounds over the cervical vertebræ is determined chiefly by the intrinsic conditions prevailing in the individual case; but it also depends to some extent upon various extrinsic forces whose action, exceptionally, is even more potent than that of the underlying gross pathological condition. These extrinsic forces, in order not to cloud the more important argument under consideration, may be dismissed by admitting, on *a priori* grounds, the hyporesonating influence of a generous dorsal musculature and adipose covering; of excessive ligamentous tension; of undue depth of the spinal groove; of spinal deformity and other diseases of the vertebral column interfering with its vibratory action under the impact of the percussion blow. Omitting, then, from further consideration these secondary influences, a number of intrinsic conditions remain to be interrogated.

The intrinsic clinical group includes lesions of the mediastinum, the lungs, and the pleura, in this order of importance, as accounting for vertebral physical signs. Mediastinal lesions, in the form of tracheobronchial adenopathies, with which this

paper deals in particular, are by far the most frequent as well as the most important of the three intrathoracic conditions mentioned, and court special attention because of the apparently paradoxical findings with which not infrequently they have a direct casual relationship. This is notably true in certain cases that otherwise afford consistent clinical data; whether relating to the history, to the mural signs, or to the radiograph. Thus, on the one hand, in one patient with urgent dyspnea, distinct cyanosis, and a radiographic picture of enlarged bronchial glands the thoracic spines may yield a sonorous hyperresonance, while, on the other hand, this region may be frankly dull and non-resilient in another patient just as characteristically hall-marked as the first one. Making due allowance for the extrinsic modifying factors noted above, the explanation of such a contradictory state of affairs should be sought by an inquiry into the anatomic peculiarities of the glandular mass and by an attempt to determine its conducting properties of the vocal and the percussion vibrations.

TONAL CONDUCTION vs. COMPRESSION DULNESS. With reference to its anatomic peculiarities, the size, the shape, and the situation of a given mediastinal mass are the main points to be investigated in connection with the physical signs. In brief, to afford any tangible signs whatever the mass must be of such a nature that it either (1) encroaches backward upon the vertebral column, or (2) acts as an intervening conducting medium—two pathologic conditions that determine diametrically opposite objective symptoms.

1. In the first instance the close impingement of a foreign body of considerable size against the mediastinal surface of the spine may effectually damp the normal vibrations thereof, and, in addition to this primary subresonating influence, may lend to the vertebral percussion sound a certain measure of its own dulness. Under such a circumstance frank dulness combined with undue tactile resistance is to be expected when the thoracic spinous tips are percussed, the conspicuousness of this external retrovertebral change being roughly commensurate with the extent of its internal antevertebral factor.

This explanation, it will be noted, presupposes the existence of a mediastinal mass close against the spine, but acoustically remote from the great air passages, and consequently in nowise concerned in the transmission of intratracheal and intrabronchial tones excited by phonation or by percussion. In the case of tracheobronchial adenopathies this condition of glandular encroachment without adequate conducting properties is, in the writer's experience, more frequent than the transmission of paraglandular tones, next to be mentioned. It must be added, however, that unlike other tumors of the mediastinal space simple glandular enlargements do not, as a rule, reach sufficient bulk extensively to

modify either the spinal or the mural vibrations of the thorax posteriorly.

2. In the second instance, that of an intervening conductor of the tracheobronchial tone, it is essential (*a*) that the glandular mass be situated so as to act as an efficient transmission path for sounds originating within the large air passages; and that (*b*) the resonance of these transmitted sounds must predominate at the thoracic segment of the spine to such a degree as to stifle any inherent dulness that the foreign body otherwise might exhibit. Here, therefore, it is to be assumed that the mass, even though it be of large size and closely abutting the mediastinal spine, also is intimately related to the trachea (or even to the gullet), so that the vibrations therein set up travel to the spine through this adenoid path, and, being comparatively the louder and the more sonorous, efface every trace of dulness. By a similar mechanism mediastinal neoplasms may hyperresonate the thoracic spine to an extreme degree—usually to a much greater extent than do simple adenoid growths—and in this connection Stradiotti's work¹⁴ on vertebral percussion in compression of the trachea by tumors of the anterior mediastinum, is of great practical interest.

The conducting properties of a mediastinal mass must be taken into account, especially when dealing with a growth firmly wedged between the air passages and the spinal column, inasmuch as such a lesion, no matter how perfectly it conforms mechanically to the essentials of a propagation tract for sound waves, cannot so act unless its histologic structure is adapted to this purpose. Other conditions being the same, a dense, compact structure under moderate tension proves a better conductor than one composed of boggy, relaxed tissue. A mediastinal fibroma is more likely to transmit tracheal hyperresonance backward than to betray its presence by merely dulling the vertebræ; on the contrary, a vascular sarcoma commonly impairs rather than exaggerates the osteal percussion resonance. Of the truth of these clinical facts, academic though they may appear, the writer has been repeatedly convinced by cases observed from bedside to autopsy. Enlarged tracheobronchial glands, although structurally ideal as sound conductors, only exceptionally form the necessary acoustic bridge from air passage to spine, and by fault of this omission must more often dull than resonate this bone. This, however, does not seem to be true of their conduction of the spoken voice, according to d'Espine's experience, which argues a clearer transmission of vocal than of percussion vibrations along a glandular route of this sort. This writer has described¹⁵ the association of pectoriloquy and striking hyperresonance over the upper thoracic vertebræ as a common finding in cases of enlarged peribronchial and peritracheal

¹⁴ Policlínico, 1911, xviii, 285.

¹⁵ Bull. de l'Acad. de méd., Paris, 1907, lvii, 167.

glands. Koch¹⁶ has found the same change in esophageal carcinoma, the inference being that the tracheal sounds were conveyed spineward by dense intervening cancerous tissue. From the study of this series of tracheobronchial cases, the constancy of d'Espine's tympany-pectoriloquy sign cannot be confirmed, although its frequent demonstration is possible, insofar as the detection of clear pectoriloquy is concerned.

SUMMARY OF RESULTS. The 18 case histories taken as the basis of this report were selected from a series of 38 mediastinal cases which afforded definite vertebral percussion findings. They represent, it is believed, typical examples of these signs, depending wholly upon the adenopathies in question and not upon the limited pleuropulmonary lesions coexisting in a few instances. No case of enlarged bronchial glands associated with some other large mediastinal mass (*i. e.*, carcinoma, fibroma, gumma) has been included in the summary, in order to rule out, so far as possible, extensive neoplastic tumors as potential factors of the spinal changes noted. Aside from the clinical histories the diagnoses were determined by the ordinary mural signs and by radiographs, most of which were the work of Dr. W. F. Manges, of the Jefferson Hospital.

The individual vertebral physical signs of the 18 tracheobronchial cases may be summarized and charted according to the following groups: (1) Interscapular dulness, above the level of the inferior scapular angles, or over the first seven thoracic spinous processes. (2) Infrascapular dulness, below the level of the inferior scapular angles, or over one or more of the five lower spinous tips. (3) General thoracic hyperresonance over the entire thoracic segment. (4) Normal percussion signs over the entire thoracic segment.

1. *Interscapular Dulness.* (Figs. 1 to 5.) To this group belong two-thirds of the series, or 12 cases, 6 affording uniform dulness to the fifth thoracic vertebræ (Cases I, III, XII, XIV, XVI, XVIII); 3, uniform dulness to the sixth (Cases VII, X, XI); and 1, dulness over the fourth, fifth, and sixth vertebræ (Case XIII). Of the 2 remaining cases of this group, 1 showed uniform dulness from the first to the seventh tips (Case VI), and the other a small basal dull patch over the sixth and the seventh vertebræ (Case XV).

In the group of six cases affording uniform dulness over the first five thoracic vertebræ (Fig. 1) but a single one (Case XIV) showed evidences of pleuropulmonary disease in addition to the mediastinal adenopathy. In this patient there was no reason to attribute the vertebral dulling to the coexisting lesion—chronic phthisis and left pleural adhesions of moderate development. Here the x-ray revealed a huge mass of enlarged glands at the tracheal bifurcation, and also many small nodules distributed through

¹⁶ *Tribune méd.*, 1912, viii, 381.

both lungs, but without cavity, disseminated fibrosis, or large consolidation. The same comment is applicable to Case XVI, one of tuberculous adenitis of the cervical, supraclavicular, and

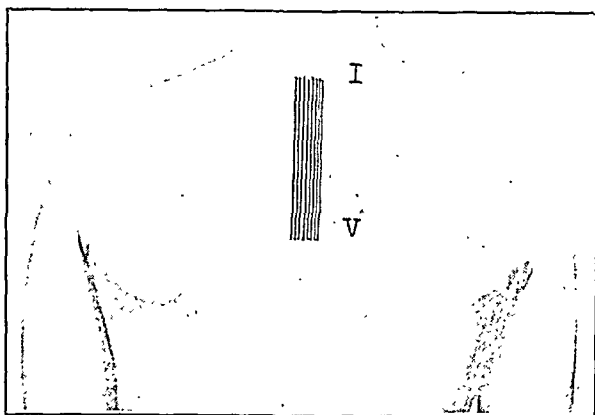


FIG. 1.—Interscapular dulness. Group of six cases, with uniform dulness and increased tactile resistance from the first to the fifth thoracic vertebra.

CASE I.—Unproductive cough; dyspnea on exertion; substernal pain and oppression for fourteen days, following a pneumonic crisis.

CASE III.—Unproductive paroxysmal cough; attacks of dyspnea; substernal pain and oppression; hoarseness. Symptoms of two years' duration, associated with numerous recurrent attacks of tonsillitis, and with a history of measles and pertussis in infancy.

CASE XII.—Unproductive cough; dyspnea; jugular fulness; facial tumefaction and venous tortuosity; substernal and interscapular pain.

CASE XIV.—Cough, with mucopurulent sputum; dyspnea on exertion; pleural pain; left-sided chronic adhesive pleurisy; chronic pulmonary tuberculosis.

CASE XVI.—Habitual dyspnea; cyanosis, venous congestion, and tumefaction of face, neck arms, and upper thoracic wall; laryngeal voice; paroxysmal aphonia and hoarseness; dysphagia. Bilateral cervical, supraclavicular, and axillary adenitis.

CASE XVIII.—Unproductive cough; habitual dyspnea; substernal oppression; dysphagia; recurrent bronchorrhea; jugular distention; venous tortuosity of neck and upper thoracic wall.

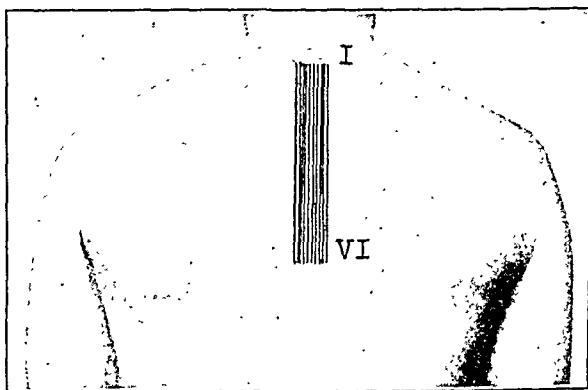


FIG. 2.—Interscapular dulness. Group of three cases, with uniform dulness and increased tactile resistance from the first to the sixth thoracic vertebra.

CASE VII.—Cough; orthopnea; cyanosis; vertigo; pleural pain.

CASE X.—Unproductive cough; dyspnea; vertigo; syncope; substernal pain; enlargement and tortuosity of superficial venules of upper thoracic wall. Chronic adhesive pleurisy.

CASE XI.—Dyspnea; cough with mucopurulent sputum; pleural pain; restricted respiratory excursion; chronic bilateral adhesive pleurisy; bilateral cervical and axillary adenitis.

axillary nodes, and with apparently normal lungs and pleuræ. The foregoing cases, then, seem fairly to represent the dulling effect of uncomplicated tracheobronchial enlargements upon the upper thoracic segment. In none of the other cases of this group was the glandular mass excessive, though in all it was an obvious finding.

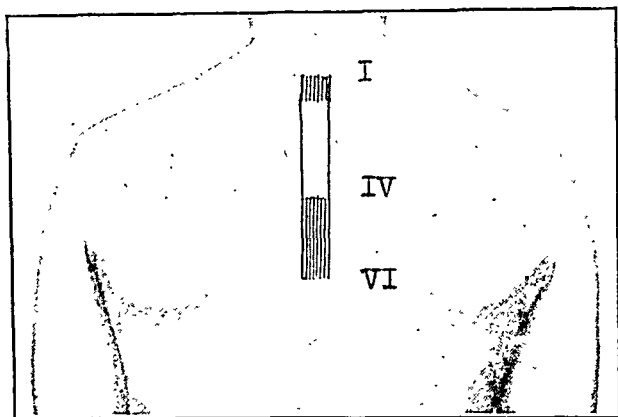


FIG. 3.—Interscapular dullness. Dullness and increased tactile resistance over the first, fourth, fifth, and sixth thoracic vertebræ; hyperresonance over the second and third.

CASE XIII.—Unproductive cough; moderate dyspnea and substernal oppression. Chronic fibroid pulmonary tuberculosis.

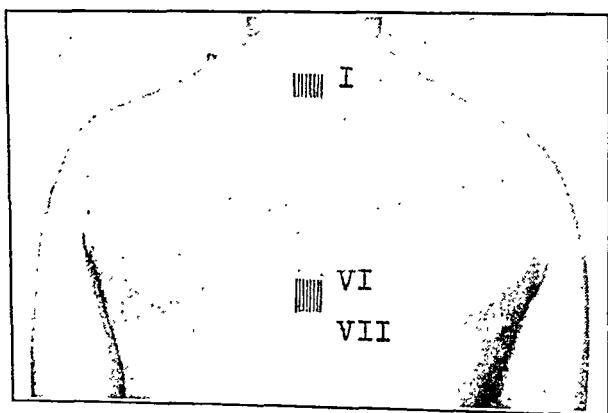


FIG. 4.—Interscapular dullness. Dullness over the first, sixth, and seventh thoracic vertebræ.

CASE XV.—Unproductive cough; habitual dyspnea; recurrent bronchitis; pleural pain. Chronic pulmonary tuberculosis, with extensive compensatory dilatation of both lungs.

Of the 3 examples of uniform dulling of the first six thoracic spinous processes (Fig. 2), 2 had generalized pleural thickening, and in 1 of these patients the cervical and the axillary glands were moderately enlarged. In all 3 the lungs were unaffected. As may be noted by the case notes summarized under Fig. 2, urgent pressure symptoms and pleural complications were conspicuous in this group, in none of which, however, did the radiograph show an extraordinary enlargement of the mediastinal lymph nodes. There is no convincing reason to account for a

lower level of thoracic dulness in these cases than in the preceding six, for the adenopathies were, if anything, of more moderate size. So in the absence of positive proof, one can but suggest as potential factors disproportionate backward growth of the affected glands, and, possibly, damping of the spinal vibrations by excessive pleural thickening and contraction.

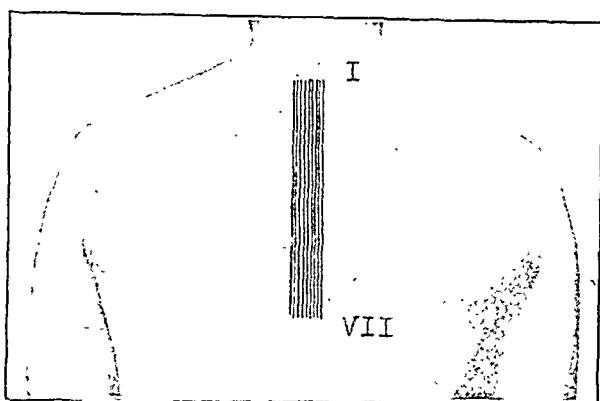


FIG. 5.—Interscapular dulness. Uniform dulness and increased resistance from the first to the seventh thoracic vertebra.

CASE VI.—Cough; dyspnea; cyanosis; substernal oppression; venous congestion and edema of the anterior thoracic wall.

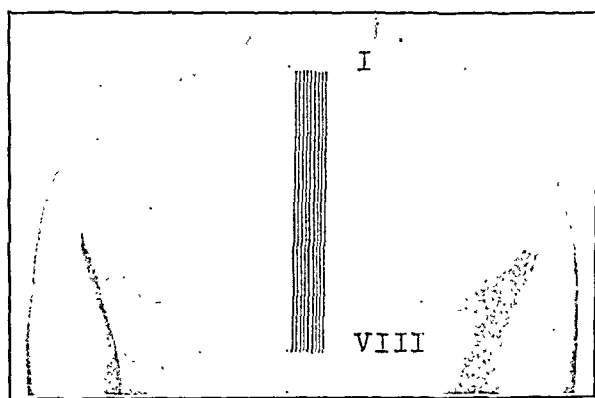


FIG. 6.—Infrascapular dulness. Uniform dulness and increased tactile resistance from the first to the eighth thoracic vertebra.

CASE VIII.—Extensive chronic adhesive pleurisy, with moderate pain, unproductive cough, and dyspnea.

In Case XIII (Fig. 3), with a patch of hyperresonance over the second and the third vertebræ, extensive compensatory dilatation of the posterior pulmonary margins was the predominant clinical feature. Case XV (Fig. 4) showed an even longer zone of spinal hyperresonance, and here also the lungs were greatly overdistended posteriorly. From these facts the association of the pulmonary and the osteal hyperresonance in casual relationship is the natural inference. In Case VI (Fig. 5) a large tracheobronchial tumor

with distressing pressure symptoms, but with normal lungs and pleuræ, was found, in combination with unbroken dulness over the upper seven vertebræ. Apparently this illustrates dulling by glandular pressure minus the modifying effects of concomitant pulmonary emphysema, pulmonary fibrosis, or pleural thickening.

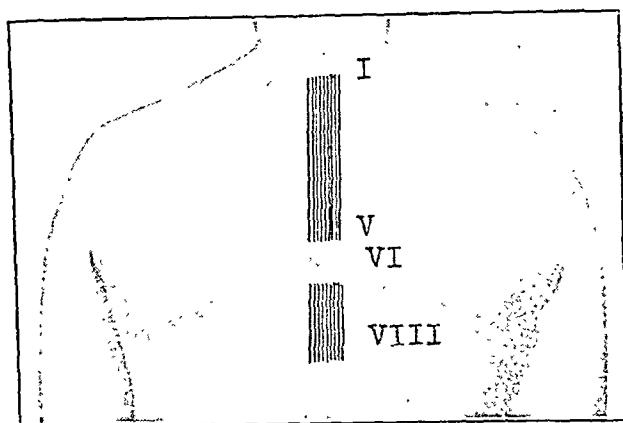


FIG. 7.—Infrascapular dulness. Dulness and increased tactile resistance from the first to the fifth thoracic vertebra, with impaired resonance over the seventh and eighth.

CASE XVII.—Unproductive cough; pleural pain; dyspnea on exertion; substernal oppression. Chronic bilateral pulmonary tuberculosis and adhesive pleurisy.

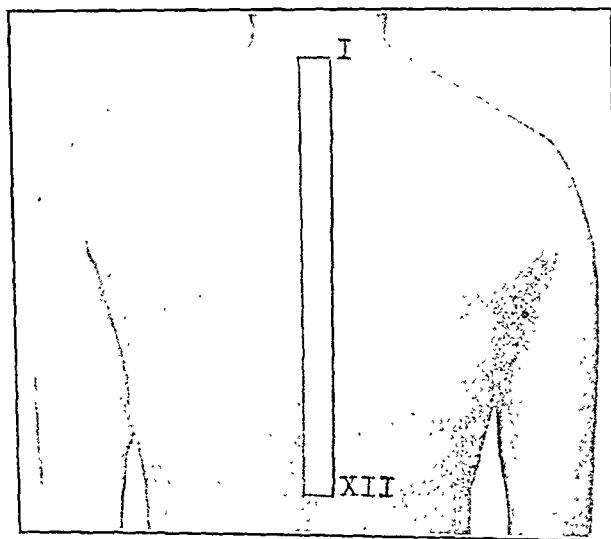


FIG. 8.—General thoracic hyperresonance. Group of three cases, with uniform hyperresonance and tactile resiliency from the first to the twelfth thoracic vertebra.

CASE II.—Unproductive cough; paroxysms of vomiting; striking dyspnea; substernal oppression for sixteen days, following a severe attack of bronchopneumonia, chiefly of the right upper pulmonary lobe.

CASE IV.—Irritative cough, occasionally attended with dark mucoid sputum; substernal pain and oppression; moderate habitual cyanosis; interscapular pain and aching.

CASE V.—Unproductive cough; dyspnea on slightest exertion; vomiting provoked by coughing; substernal pain and oppression; chronic follicular tonsillitis. Symptoms of four years' duration, and first observed a few months after recovery from diphtheria.

2. *Infrascapular Dulness* (Figs. 6 and 7). In the two instances of dulness below the level of the inferior scapular angles the zone

of hyporesonance over the first eight thoracic vertebræ was uniform in one case (Case VIII) and interrupted by a resonant sixth vertebral tip in the other (Case XVII). In both patients the glandular enlargement was accompanied by extensive pleural adhesions, and in one by bilateral pulmonary tuberculosis, neither of which conditions seemed satisfactorily to account for the spinal signs.

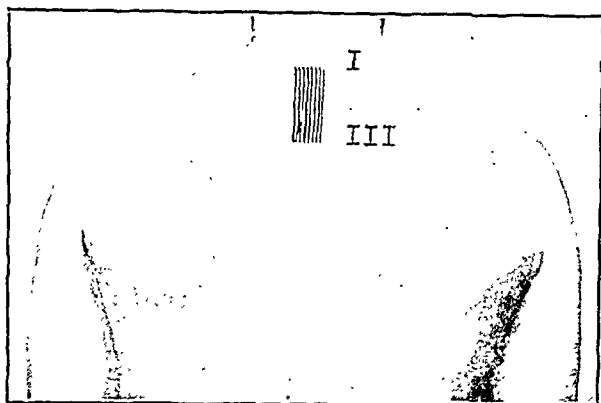


FIG. 9.—Normal thoracic percussion signs. Impaired resonance and slightly increased tactile resistance from the first to the third thoracic vertebra.

CASE IX.—Painful, unproductive cough; restricted respiratory excursion; habitual dyspnea; cardiac hypertrophy; left-sided chronic adhesive pleurisy.

3. *General Thoracic Hyperresonance* (Fig. 8). In the three cases belonging to this group (Cases II, IV, and V) it is fair to attribute the spinal hyperresonance solely to direct conduction of the tracheobronchial tones by the intermediation of the adenoid masses. These were of large size in all three cases, and in none did either emphysema or pleurisy coexist. Dry cough, persistent dyspnea, and great substernal oppression were common symptoms, and hyperresonance of the whole thoracic segment was the common physical sign in these three examples of uncomplicated adenopathy.

4. *Normal Percussion Signs*. In one patient of the series (Case IX, Fig. 9) no impairment of resonance below the level of the third thoracic spine was detected, despite Röntgen proof of the glandular enlargement, and notwithstanding clear mural signs of left pleural adhesions and of cardiac enlargement. Even Ewart's "isolated (ninth) dull spine" was unmistakably resonant, as well as the several processes above it, directly back of the heart and its great vascular trunks. No explanation of the lack of vertebral signs can be hazarded in this instance.

CLINICAL VALUE OF CHANGES IN SPINAL RESONANCE. A review of the foregoing data, considered in the light of results obtained in numerous other mediastinal lesions, warrants the following conclusions as to the clinical utility of vertebral percussion in the group of cases under discussion:

In simple enlargement of the tracheobronchial lymphatic glands percussion of the thoracic vertebræ, especially above the level of the inferior scapular angles, usually affords tonal changes of real clinical value if properly interpreted. These changes, more often corroborative than primarily diagnostic, invariably should be correlated with the mural signs of the individual case.

Hyporesonance with maximum tactile resistance and hyperresonance with minimum tactile resistance may have precisely the same significance in uncomplicated adenopathies. To explain this seeming paradox it is to be assumed that in the former instance the mass exerts a dulling pressure, and that in the latter it conducts the predominant tracheal tone. In glandular enlargements associated with pleuropulmonary lesions, emphysema and pleural adhesions are to be reckoned with as additional factors of hyperresonance and hyporesonance respectively.

In comparison with other (neoplastic) mediastinal masses, tracheobronchial tumors affect the vertebral percussion sound to a minor degree and more often produce dulness than hyperresonance. This general rule has a restricted clinical bearing in bearing in differentiating adenoid and malignant tumors.

In routine examinations ordinary mediate finger percussion is preferable to instrumental pleximeter percussion in studying vertebral changes of sound. The latter method gives no surer clue to tonal changes than that afforded by percussion with the bare fingers, and its practice obviously forbids all judgment of tactile resistance.

THE TRANSMISSIBILITY OF THE LEPROBACILLUS BY THE BED-BUG (*CIMEX LECTULARIUS* L.).

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THE following paper was presented before the Philadelphia County Medical Society, on April 20, 1912, but publication has been withheld because of a desire on the part of the writers to more

fully study the strain of organisms employed in the transmission experiments, for reasons indicated in the text. Such study has been continued, but a final conclusion has not as yet been attained, although the writers now, as at the time of presentation of the paper, incline to regard the chromogenic acid-fast organisms used in their studies as true leprosy bacilli and to look upon the supposedly contaminating non-acid-fast elements of the same morphology in the cultures as identical, but representing another phase of a pleomorphic organism. A recent statement by Kerr,¹ implicating the bed-bug as a conveyor of leprosy, has led the writers to no longer postpone publication, but to leave to a subsequent time a fuller discussion of the specific status of the organisms employed in their experiments in transmission.

In preface the writers would acknowledge that the uncertainty prevailing in respect to the specific status of various cultures regarded in different laboratories as *Bacillus lepræ* must necessarily postpone decision as to the value of the laboratory studies in transmission herein recorded. While it is commonly stated that the work of the earlier investigators in attempt to cultivate Hansen's bacillus, employing only the ordinary laboratory media, was without result, it will not improbably be necessary in making up a final decision upon the question of the specific characteristics of the true leprosy organism to carefully review all of their data. The recent workers, however, as Rost² and Williams³ in India, Clegg⁴ in Manila, Duval⁵ in New Orleans, and others, have uniformly obtained organisms which in the tube appear as yellow to orange chromogens, which are acid-fast, and which vary in minute morphology from a bacillary to a coccoid form. All of these workers seem to have attained readiness of growth by utilizing culture media in which advanced protein cleavage products constitute an important part, as the extract of putrid fish employed by Rost and by Williams, the medium of Clegg in which by prior seeding with colon bacilli and amebæ the products of hydrolytic splitting were present, the deliberate addition of tryptophane to the medium by Duval, or the preparatory trypsinizing of the medium by the last-named writer and others following him.⁶ It is true that certain differences between the strains obtained by these investigators have been urged, but the main features of

¹ United States Naval Bulletin, 1912, vi, 316; reference in editorial in Jour. Amer. Med. Assoc., November 16, 1912, lix, 1798.

² British Med. Jour., 1905, No. 2302; Scientific Memoirs by Officers of Medical and Sanitary Departments, India, 1909, N. S., No. 42.

³ Scientific Memoirs by Officers of Medical and Sanitary Departments, India, 1909, N. S., No. 42.

⁴ Philippine Jour. Sci., April, 1909, Series B, iv, 403.

⁵ Jour. Exper. Med., September, 1910, xii, 649.

⁶ Duval, Jour. Exper. Med., March, 1911, xiii, 365; Smith and Rivas, New Orleans Med. and Surg. Jour., October, 1912.

chromogenic character, acid-fastness in staining and bacillary to coccoid morphology, are common to all of these strains cultivated from leprotic tissue in media having amino-acids as a definite element in their composition in widely separated places by independent workers. No little doubt as to the real status of such growths and the purity of cultures has, however, arisen from the uncertainty of experimental inoculation, and the invariable presence of organisms in the cultures which have been usually looked upon as contaminations or perhaps symbiotic organisms possibly of importance. These are by no means of constant characteristics. They are usually of the same morphology and size as the ordinary acid-fast bacilli, but are non-acid-fast; again, mycelioid growths appear, some acid-fast, some non-acid-fast. (More recently Duval⁷ has urged above his original chromogenic organisms a nonchromogenic acid-fast bacillus as more probably the true *Bacillus lepræ*.) Final determination of both these points is lacking, that is, the verity of existing cultures and question of contamination. In the opinion of the writers there exists an important question in the point raised by Williams⁸ as to whether in reality the causative organism of leprosy is not pleomorphic (a streptothrix in his suggestion), with varying phases which include the supposed cultural contaminations. The writers incline to credit this suggested pleomorphism for reasons to be stated elsewhere, and are of the opinion that the cultured organisms used in the following study (one of Duval's original strains) are lepra bacilli, in spite of the fact that in every tube, as demonstrable in stained films, at least a few non-acid-fast organisms of the same morphology as the acid-fast ones were found, and that, moreover, inoculations into guinea-pigs and rats gave but doubtful or negative results. Even, however, should this experimental phase of the study prove valueless because of the employment of bacteria which may eventually be shown to be non-specific, the second phase of the work, inculcating the bed-bug or obtaining lepra organisms when withdrawing blood from a leper, is of interest, and should be recorded.⁹

Laying this problem aside for the time, with clear understanding that in a part of the studies dealt with there is room for legitimate question because of the unproved status of the strain of bacteria employed, a brief discussion of the prominent views upon the mode of acquirement of leprosy is desirable in introduction.

From the earliest references of religious and historical writings to the affection a belief in direct contagion without intermediary has held tenacious sway, personal contamination of the clean by

⁷ Jour. Cutan. Dis., July, 1912, xxx, 389.

⁸ Indian Med. Gaz., Supplement, May, 1911; see also Deycke, V Internat. Derm. Kongr., September, 1904, Band i, p. 385 (Ref. Centralbl. f. Bakt. u. Parasitenk., xxxvi, 662), and Deycke and Reschad, Deutsch. med. Woch., 1905, xiv and xv (Centralbl. f. Bakt. u. Parasitenk., vol. xxxviii, Ref., 415).

⁹ See Kerr, *supra cit.*, and Long, *infra cit.*

the leper being guarded against by stringent laws. Nevertheless, in modern times the insufficiency of such views has been a marked feature in scientific expositions of the affection; and no man of experience with leprosy today but recognizes the fact that quite commonly long and even intimate association of unclean and clean may fail to establish contamination. Isolated cases in families, sometimes large families closely associated because of crowding of the dwelling, are the rule rather than the exception, and commonly the effort to trace the source and route of infection in such individuals is futile. Under this same heading are ordinarily meant by the populace, and may here be included, infection by actual bodily contact, by special sexual contact, or by contact with ordinary inanimate objects contaminated by a leper, as clothing, common utensils, and similar objects. That occasionally transmission of the causal agent of the disease is in some such manner actually accomplished has certainly not been disproved; and that it may sometimes thus take place may be accepted as a matter of possibility and probability. But there is little evidence that such direct transmission is the rule. Were it even moderately common, infected families should far more frequently furnish multiple cases than is known; attendants and nurses in leper hospitals should show a higher proportion of infection in their number; the recognition of the source of infection should frequently be possible, and appreciation of the time and mode of transfer should often be clear.

The older conception of the disease clearly included the idea that respiratory transmission is possible, expressions indicating the danger of breathing in the exhalations and atmosphere close about a contaminated subject being not infrequent in the older writings. The clinical observation¹⁰ of the frequent presence of Hansen's bacilli in the nasal and oral mucus lent in recent years some added weight to the revived belief, but again the proposition fails of actual proof. It is altogether probable that there is dissemination of the essential microbes with the nasal and oral discharges to the surroundings of the leper, but we are ignorant of the fate of such discharged bacilli. Were the subsequent step of infection merely that of inhalation the same arguments demanding a probability of more frequent infection of those about leprous subjects should prevail. The appearance of the bacilli in the nasal secretions is really no earlier than in other excreta and in other parts of the same cases; and their early recognition in the former is by no means valid evidence that the nose is the primary point of infection. While the possibility of this mode of transmission cannot be set aside completely, its acceptance can at best be only tentative, and certainly not to the exclusion of other and more probable methods.

¹⁰ Bibliography in AMER. JOUR. MED. SCI., November, 1894, p. 541; Sticker, Münch. med. Woch., 1897, No. 39, p. 1063, and No. 40, p. 1095; Schäffer, Arch. f. Derm. u. Syph., xlv, 159.

Even before Hansen's discovery of the bacillus of lepra the chance of acquirement of the disease by alimentation had been proposed. The eating of fish, especially of putrid fish, of spoiled cheese, oils, excessive indulgence in pork, and a variety of other foodstuffs was at one time urged, but always without acceptable data. In the latter part of the past century Sir Jonathan Hutchinson¹¹ revived the theory of acquirement from the eating of fish, but in spite of his authority and his plausible arguments there was but slight credence yielded to his views. There must be decided satisfaction to Sir Jonathan in the success of Duval and his associates,¹² which the writers do not hesitate to confirm from their experience, in readily infecting fish (in which inoculation with cultures of *Bacillus lepræ* is rapidly followed by a wide appearance of the acid-fast organisms in the various organs of the body, even though definite nodular inflammatory reactions are not found and the fish remain indefinitely apparently unharmed). It is said that when leprosy is endemic and the drainage carries the discharged lepra bacilli into a quiet sea arm the fish in the latter have been found leprous. The writers are inclined to agree with Couret¹³ and Duval that fish and other cold-blooded animals, as turtles and snakes, may represent the true habitat of the lepra bacillus, and that warm-blooded animals, including man, are relatively or absolutely resistant and require either special dosage to insure infection or special natural or acquired predisposition to become leprous after the introduction of the bacilli. That infection from infected and uncooked or imperfectly cooked fish, either from the introduction of the bacilli into wounds of the oral or esophageal mucous membrane made by fish-bones or by gastric or intestinal inoculation through abrasions or absorption, does not in this light seem very improbable. (In a number of carefully studied early cases of human leprosy there has been noted profuse dissemination of the bacilli in the internal organs without focal lesion, as in the spleen and liver, at a time, too, when the skin showed no gross change; which may be an argument to one who does not regard the disease as primarily a general one that primary inoculation was more likely internal than in the skin. For that matter the same suggestion may as well be accepted from the occurrence of the so-called initial fever of leprosy, appearing before any skin lesions are apparent by our present modes of observation.) That popular belief holds that the use of rotten fish is particularly dangerous in this connection is singularly substantiated by the fact that the cultivation of the bacilli of leprosy in the laboratory is favored

¹¹ *Med. Times and Gaz.*, October 30, 1867; *Med. Press and Circ.*, July 8 and August 11, 1880; *Lancet*, London, 1880, No. 13; *British Med. Jour.*, March 22, 1890; *Leprosy and Fish-eating*, London, 1907.

¹² Couret, *Jour. Exper. Med.*, May, 1911, xiii, 576.

¹³ *Loc. cit.*

by media containing the products of digestion and cleavage of proteins.

The writers are unwilling at this stage of our knowledge to further advocate the theory of Hutchinson, but believe it worthy of more careful study than has been accorded it in the past; and should the acid-fast chromogenic bacilli here involved actually prove to be the true pathogenic agents of leprosy, would accept the idea as a probability for at least some cases of human acquirement.

Whatever credence may tentatively be granted to any one or all of the suggestions thus far outlined, brief reflection must surely lead to the conclusion that no one, or the whole group together, can satisfactorily explain the acquirement of the affection in all or even in any large proportion of the instances of the diseases in natural conditions. Supposing fish-flesh to be a conveyor of leprosy to human beings, there are nevertheless many localities in which the disease prevails, but where fish constitute only a rare article of diet, if ever used. If respiratory acquirement be possible, it is open to reasonable doubt that this can be a prevailing mode when one recalls the comparative infrequency of infection of relatives and attendants in homes and institutions inhabited by lepers and the common appearance of the disease in persons who do not recall exposure to lepers; and the same statements are *apropos* to the idea of direct contagion.

These evident inefficiencies of the more prominent attempts to explain the acquirement of leprosy, with comparative reflection upon the vagaries of such acquirement, and the peculiarities of insect transmission of a now rapidly lengthening list of diseases, urged upon the minds of the writers the chance of some living and moving agent, as an insect, enacting the role of a transmittor. The idea of possible insect convection is not new, although it was arrived at by the writers entirely independently. Castellani and Chalmers¹⁴ refer to Nuttall as pointing out that Linnaeus and Rolander regarded a fly (*Chlorops lepræ*) as the active agent of transmission from one human being to another; that Corredor suspected flies in general; Joly, *Sarcoptes scabiei*; Sommer, mosquitoes. The same writers state that Goodhue demonstrated leprosy bacilli in *Culex pungens* and in the common bed-bug; and that Marchoux and Bournet suggested some of the simuliidæ as carriers of the disease. Walter Brinkerhoff,¹⁵ while Director of the Leprosy Investigation Station of the United States Public Health and Marine Hospital Service at Honolulu, called attention to Goodhue's discovery of the bacillus in the body of *Culex pipiens*, and to a similar discovery by Mr. John R. Taylor in the stomach of a mosquito which had previously bitten a leper in Las Animas Hospital

¹⁴ Manual of Trop. Med., New York, 1910, 1st ed., p. 839.

¹⁵ Note on Possibility of Mosquito Acting in Transmission of Leprosy, Public Health and Marine Hospital Service of the United States, 1908, p. 23.

in Havana; and comments upon the possibility and possible method of transmission by mosquitoes. After the work of the writers was well advanced the note of E. C. Long,¹⁶ of Basutoland, was encountered by us. Long states that in his study he collected bed-bugs from huts where no leprosy existed and allowed them to bite lepers in the vicinity of leprosy nodules of the face. The bugs being killed and the alimentary tract and its contents examined, "in every bug that bit freely a bacillus was found, which in shape, size, and staining reactions is similar to the *Bacillus lepræ*." He also cites the case of a native of Basutoland, who came from a village free from leprosy and who had no lepers among his relatives, but who in a village fifty miles from his home had spent a single night in a hut from which recently the solitary leper of this second village had been expelled. During this night he was severely bitten by bed-bugs, and within a year the lesions of leprosy appeared upon him.

Impressed with the chance and the compatibilities of the idea of insect transmission (which impression was later confirmed and strengthened by the statements above mentioned) the writers instituted a study to determine the problem. At first, merely as a preliminary observation, it was determined positively that it is possible for ordinary house-flies, carrying the bacilli, as they are known to carry a variety of organisms on the exterior of their bodies, to convey the infection to fresh media. The flies were placed in glass vessels containing various substances, as sugar solution, blood, etc., previously contaminated with leprosy bacilli from culture tubes (one of Duval's strains). After the flies had crawled over or through the contaminated material and tasted of it the bacilli were readily obtained both by staining and by culture from the proboscis and from the legs. No evidence was obtained, however, that the bacilli were taken into the alimentary canal of the fly. A number of the insects after having been seen to feed upon the contaminated material were killed, their legs, wings, and heads removed, the exterior of the body well washed in disinfectant solutions, and in the smears made from the thorax and abdomen thus prepared no organisms comparable morphologically and tinctorially to *Bacillus lepræ* were discovered.

The main investigation was, however, from the first directed to the common bed-bug (*Cimex lectularius* L.) because of its ubiquity, close relation with man, and its commonly believed but unexplained preference for some individuals and avoidance of others in the same groups. For a long time, beginning in the fall of 1911, attempts to induce the bugs to ingest blood to which bacilli from the culture tubes had been mixed, failed, and at this time there were no lepers available upon whom the bugs could be fed. After

¹⁶ Arch. Middlesex Hospital, Clinical Series, August, 1911, viii, 49; British Med. Jour., 1911, ii, 470; Jour. Trop. Med., 1912, xv, 72.

numerous failures it was found that if the blood (using citrated blood of dogs) with admixed bacilli were placed in a suitable dish and covered with a piece of fresh skin the bugs would bite through the skin and suck up the artificially infected blood.¹⁷ At first dog skin was used, but was found too thick, and rat skin was thereafter employed. With the thicker skin, not easily penetrated by the proboscis of the insect, two bugs out of a dozen were found to contain bacilli; but with the thinner rat skin all the bugs except the very small ones succeeded in reaching the blood and became infected. The hair is shaved off the skin and the latter stretched over the blood in the dish, its under surface in direct contact with the blood; and the dish thus prepared is kept warm in the incubator, the bugs being applied in the incubator chamber under an inverted test-tube. Smears made from the excised alimentary canals of unexposed bed-bugs were invariably free from acid-fast bacilli. Smears made from the bugs immediately after biting, as a rule, showed but few bacilli, and those of the coccoid form which had been mixed with the blood from the culture-tube. From observations made upon over one hundred infected bugs there is no doubt in the minds of the writers that for a time the bacilli increase in size and also in numbers within the bed-bugs. They elongate into typical bacillary form, and in sections of bed-bugs may be found, at least between the third and tenth days after feeding, not only in the alimentary canal but also in the various glands of the head, thorax, and abdomen. They are not numerous in the glands, but in the series examined have been repeatedly found in these locations. After a time they disappear from the bugs, the time of disappearance varying between two weeks and thirty or more days. The mode of disappearance is probably not a simple one, some of the bacilli being found discharged with the fecal matter, others apparently broken up in the bugs into fine acid-fast granules.

After this stage of study had been reached, fortunately for the work, it became possible by the kindness of the staff of the Municipal Hospital for Infectious Diseases, through Dr. J. A. Kolmer, pathologist to the institution, to feed bed-bugs directly from two lepers who had been received in the hospital a short while previously. In smaller numbers, but indubitably, acid-fast organisms of the usual human type of lepra bacilli were found in a number of the bed-bugs which had fed upon these subjects, but not in all. From further study of these human cases the writers are persuaded of the existence in lepers of a true lepra bacillemia, the bacilli being obtained both by culture and by staining (blood citrated, laked,

¹⁷ A personal statement to one of the writers by Professor Nuttall was recently made which easily obviates this difficulty. If the antennæ of the bed-bugs be removed by section with fine scissors or destroyed by a hot point there is no hesitation on the part of the insects to suck in any material offered.

centrifugated, and the sediment spread and stained) in blood removed directly from the veins without contact with the skin lesions. This belief is further urged by the fact that lepers constantly show the organisms in the various secretions and in the internal organs as well as in the dermal lesions. It seems quite possible to think that failure to acquire the organisms by the biting bugs, when it is recalled that similar failures were noted in the laboratory feeding through the thick skin of the dog, may have resulted from mechanical difficulty of penetration through the thick leprous skin to a suitable capillary (the bacilli in the fixed tissues being probably less readily acquired than those in the circulating blood). It is easy to surmise tentatively, in partial explanation of the rarity of infection of entire family groups by bed-bug transmission from a given leper in the family, that only the well-gorged bugs are likely to contain bacilli; that these are not likely to again feed for a number of days, and in the meantime may have lost their bacilli as above shown; that, following the observations above noted, perhaps in not all cases do the bacilli gain access to the salivary glands and tubes of the bugs, and that failure of transmission at the next feeding may sometimes depend upon this feature; and that, therefore, even disregarding possible individual immunity from the bed-bug or special individual resistance to lepro bacilli by given human beings, it is not to be expected that leprosy should invariably follow the bite of a bed-bug which has previously fed upon a leper.

The well-known difficulty and questionable results of animal inoculation thus far reported by various writers have interfered with the determination of the final link of the chain of reproducing the disease in appropriate animals by permitting infected bugs to bite such subjects. Guinea-pigs, Japanese dancing mice, white mice, and monkeys have been employed with varying success by different investigators; and it is well known that among the cold-blooded animals fish, turtles, and snakes have been found suitable subjects for the growth of the bacilli, but do not exhibit histological changes from the presence of the bacilli in the economy. In inoculation studies with mammals in this laboratory guinea-pigs and white rats have been used. Thus far no results whatever have been attained in rats, which apparently are completely immune to the strains of lepro bacilli in our possession, no matter what the dosage. Duval's¹⁸ suggestion that previous sensitization of the experiment animal by injection of dead cultures or the lepro bacillary protein has recently been followed, but as yet no results have been attained either in guinea-pigs or rats. One of two original guinea-pigs inoculated without sensitization last summer with one

¹⁸ Duval, Jour. Exper. Med., August, 1911, xiv, 181; Duval and Wellman, Jour. Infect. Dis., July, 1912, xi, 116.

of Duval's strains showed in the inoculated leg a swollen inguinal gland, from which and from a small nodule at the site of inoculation acid-fast bacilli and lepra cells containing bacilli were obtained when the animal was killed. Of more than twelve warm-blooded animals either directly inoculated or bitten by infected bed-bugs this single successful result can at this time be recorded. Thinking that cold-blooded animals would perhaps lend themselves better for the biting experiments attempts to get the infected bugs to bite fish and frogs have been made; but it has been impossible to induce the bed-bugs to bite fish at positions where scales were removed to permit penetration. Several frogs after many trials were apparently bitten (the bugs puncturing through a bit of rat skin into the frog, but never showing any inclination to feed on the uncovered frog). In none, however, were bacilli found after natural death or after sacrifice.¹⁹

In despair of actually producing the disease by the bite of infected bugs in the available experiment animals, it was sought to find at least whether in biting there takes place a discharge of the lepra bacilli along with the mouth secretions of the bug into the wound. The tiny site of puncture into the skin of guinea-pigs and other subjects was at once excised for examination. In serial sections of several of these minute bits of epiderm and corium the writers have failed to find any bacilli, but five times in fresh smears of the crushed skin from a group of eleven attempts made in this wise, small bunches of acid-fast bacilli have been found, in four of the five controlled by negative findings in smears similarly made from tissue in the immediate vicinity and from the surface. From their appearance the writers believe these to be lepra bacilli transferred to the experiment animal by the bite of the infected bugs. That no more uniformly successful results have been attained by the writers is not to be regarded a matter of much surprise, as it is to be recalled that at the time of biting there may have been in the oral glands of the bug none of the bacilli, and that further, the technical difficulties in finding the small numbers of bacilli deposited in the line of puncture into the skin are very real; but so far as it goes there seems to us little room for doubt that an actual transference was accomplished.

In conclusion, always with reservation occasioned by the uncertainty of the pathogenic value of the bacilli employed, the matter of these preliminary studies may be summarized as follows:

1. Bed-bugs can be induced by methods detailed to take up lepra bacilli with blood to which the bacilli have been added.

2. Within the bugs for a time the bacilli increase in size and apparently in numbers, but eventually disappear, partly by dis-

¹⁹ All the animals here referred to have remained for months without appreciated infection, and when killed showed no bacilli in spreads from blood and internal organs. This is true of both inoculated and bug-bitten experiment animals save as above recorded.

charge with fecal matter, partly also by disintegration within the bed-bugs.

3. Within the bugs thus infected the writers have found the bacilli in the glands as well as in the alimentary canal.

4. Bed-bugs acquire lepra bacilli also with blood taken from human leprous subjects, but not invariably.

5. Bed-bugs infected in the laboratory, and presumably more certainly and more heavily infected than those which are infected from human beings, may transmit the bacilli by route of the sucking apparatus to the skin of the animal bitten.

6. Whether thus the disease is transmitted in nature, that is, whether the organisms are unchanged and of sufficient virulence to induce leprosy, remains to be proved; and the writers would here also indicate their belief that if bed-bugs really do transmit the disease, as they suggest, they are probably only one of a number of possible conveyors, other types of biting and sucking insects being equally open to suspicion (particularly those which regurgitate in biting).

SYRINGOMYELIA: WITH AUTOPSY FINDINGS IN TWO CASES.

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THE development of cavities in the spinal cord following apoplexy, traumatic hemorrhage, myelitis, embolic processes, or primary degenerations of the nervous tissues have not infrequently been described. In a number of instances in which a primary causative factor had been suggested for the condition the authors indicated that an inflammatory process and reactive gliosis had occurred secondary to the development to the cavity. The type of cavity developing in the cord is different in many cases, and this has led to a number of theories concerning the mode of origin. Moreover, the clinical history of the onset of these cases in adults is so divergent that it would appear that more than one factor was concerned in their development.

The majority of cases of syringomyelia have been described in association with gliosis, or as some prefer to call it, a diffuse glioma. Much attention has therefore been concentrated on this aberrant tissue of the cord. True gliomas of the cord without the presence of degeneration and cavity formation are known, while, on the other hand, there have been cases in which the development of a local or extensive cavity in the cord has been unassociated with primary changes in the glia.

The relation of syringomyelia to true tumors is particularly important in those cases where the gliomatous processes can be demonstrated to precede the cavity formation. In these conditions there is a definite mass of invading tissue which extends longitudinally in the cord and commonly involves the gray matter and the posterior columns. It would appear that the growth had its origin in the glia of the gray matter, but its subsequent extension not infrequently invades the white matter of the cord, where it displaces the various tracts.

The involvement is generally greatest in the posterior columns, but the tumor need not be confined to this region. Thus the entire cord may be infiltrated and destroyed in one segment, leaving little or no normal tissue, while in the segments both above and below this area the new-growth is confined to the tissues behind the commissure. At different periods of development the gliomatous mass may undergo softening, with partial absorption of the liquefied area. This softening is usually most extensive in the area of the greatest tumor involvement and in the areas of the cord occupied by the secondary growths. The absorption of the softened matter may lead to the complete disappearance of the cord in one or more segments. In other instances the main gliomatous mass continues to extend almost as rapidly as the central softening, with the result that the cord is occupied by a considerable tumor mass with an inner cavity. From the area of primary softening a similar process of degeneration follows the central portion of the infiltrating gliosis. Thus the column of new-growth occupying the posterior tracts comes to have a tubular cavity passing through it. Where the extension of the gliosis or tumor has followed several nerve tracts there may occur separate channels of softening. The process of softening is also accompanied by degenerative changes of the cells and tissue immediately surrounding the tumor tissue. Several investigators have indicated that the process of degeneration is associated with certain vascular changes as well as pathologic conditions in the enveloping membranes.

Under the general consideration of syringomyelia is included the discussion of cavity formation resulting from congenital anomaly. Such conditions are observed in cases where the spinal canal has been improperly closed, leading at times to the formation of a diverticulum which is still in communication with the spinal canal or where a channel near the posterior sulcus is independent of the central canal, and in no way communicates with it. Cavities of the former type are lined with a layer of columnar cells simulating the ependyma. It must, however, not be inferred that all cavities having such a lining membrane are of congenital origin. Some of the lesions of later life appear to acquire a similar lining.

The cases which are of the most interest are those which develop in adult life or at least in whom the symptoms first appear at this

time. These cases have led to repeated controversies as to the primary factors in their origin.

Although, clinically, a group of symptoms indicative of syringomyelia has been described, not a few cases found at autopsy have presented symptoms of quite another character.

The following two cases of syringomyelia are of interest in indicating the mode of origin of their cavities, in the one case with and in the other without the presence of tumor.

CASE I.—Mrs. R. M., aged thirty-eight years; housewife. The patient was admitted to the Pittsburgh Hospital September 19, 1910, under the service of Dr. J. D. Heard, to whom I am indebted for the clinical history.

On admission the patient complained of pain in the lower abdomen and along the spine, and inability to move the legs. The patient was the mother of nine children, and had been a healthy woman until last fall, when, after nursing her husband through a prolonged fatal illness she broke down. Moreover, at this time a number of subcutaneous abscesses developed in various parts of the body. Associated with this infection she had an acute attack of pain (acute pleurisy) in the left chest, which confined her to bed. She gradually improved, so that she was able to be up until the morning of her admission to the hospital. Suddenly upon that morning she found herself unable to move either leg. She was very definite in stating that this complete paraplegia took place within a period of two or three minutes. Since then the paraplegia has been complete. The patient was an emaciated female. There was a complete paraplegia, with loss of reflexes below the waist line. The bladder was distended to a point about an inch below the umbilicus, and contained 1000 c.c. of urine. Anesthesia was complete to all forms of sensation over the surfaces below a transverse line 3 cm. above the umbilicus. The left pleural cavity was the seat of effusion, which reached to a point opposite the seventh rib posteriorly. This effusion was rapidly absorbed, leaving behind an impaired percussion note.

Nervous System. Complete anesthesia over the area mentioned, which persisted until the end. There was no shifting or extension of the original area. The patient was never able to make the slightest voluntary movement of the legs, but during the last two weeks of her life, involuntary twitchings occurred in the anterior muscles of the thigh. There were marked trophic disturbances. Decubitus appeared over the sacrum about six days after admission. This spread rapidly, the tissue literally melting away. At the time of death ulceration had extended to the bone and measured 10 x 12 cm. There was also one over the inner side of the left foot and also an ulcer over the left hip. Control of the bladder or rectum was not regained. The urine toward the last became excessively fetid.

Laboratory Findings. The Wassermann test for lues was negative. Albumin was constantly present in the urine. From the first, granular casts, pus, epithelial cells, and occasional red blood cells were found. Leukocyte count varied from 12,000 to 21,400.

Clinical Diagnosis. The sudden appearance of the manifestations suggested the diagnosis of hemorrhage into the cord. Death was caused by pneumonia, sepsis, and exhaustion. An autopsy was performed one and a half hours after death.

Autopsy. The body was that of a middle-aged woman, 165 cm. tall. The skin surfaces were pale and the body was considerably emaciated. The pupils were narrow, the right being slightly larger than the left. Extensive and deep decubitus ulceration was seen over the sacrum, which extended to the bone, and measured 10 cm. x 12 cm. A round punched-out ulcer was seen over the left hip, exuding pus. A small fibroma was present in the skin of the right side of the neck. Some superficial ulcers were found over the heels and one over the inside of the foot. The genitals were negative. A small amount of blood exuded from the vaginal orifice. There was no postmortem rigidity of any of the muscles.

Thorax: No excess fluid was found in either pleural cavity. Some old adhesions were seen over the apex of the left lung and along the posterior border of the right lung. On bringing forward the left lung the lower lobe felt solid and was firmly adherent to the posterior thoracic wall. On removal the lung substance was torn by the adhesion. There was some purulent exudate enclosed by the adhesions behind the lung. This exudate was seen to burrow behind the parietal pleura and enter the intercostal space between the eighth and ninth ribs. An opening 1 cm. in diameter was seen in the pleura. Behind this opening was a larger cavity, from which pus could be expressed. This cavity was immediately over the angles of the ribs, and extended up and down, being 7 cm. in length. The ribs which formed the posterior boundary of this cavity were eroded on their inner surfaces. The pus cavity was 4 cm. in width and advanced to the bodies of the vertebræ. The right pleural cavity also showed some dense adhesions behind the posterior border of the lung, while in the retropleural tissues opposite the angles of the seventh, eighth, and ninth ribs was a shallow abscess cavity almost identical in size and appearance to that on the left side. These two abscess cavities had paths of communication across the vertebræ. The eighth and ninth ribs as well as the vertebræ opposite the abscess in the right side were denuded of their periosteum. There was a distinct lateral curvature to the left of the dorsal spine beginning at the seventh dorsal and ending at the first lumbar. The internal viscera showed nothing particularly of interest. A septic pneumonia was found in the upper lobe of the left lung. Extensive suppurative processes were present in the kidneys and urinary tracts.

Cord: On removing the cord some pus was noted about the vertebræ and on the outer surface of the dura in the region of the intervertebral foramina of the seventh, eighth, and ninth dorsal segments. The dura was decidedly thickened in this region. There was no evidence of inflammation nor of pus within the dura mater. The pia was seen to be free from adhesions and exudate. Above the eighth dorsal vertebræ the cord was normal. Opposite the eighth and the upper part of the ninth dorsal vertebræ the cord did not present its normal contour, but instead of being firm and round it was soft and completely flattened. The flattening was due to the loss of the structure within the membranes. The pia mater over this area showed some injected vessels. The cord when cut through at the upper border of the ninth dorsal was disintegrated and structureless, and exuded a yellowish creamy material looking not unlike pus. Sections through the cord opposite the fifth, sixth, and seventh dorsal vertebræ showed the cord structure fairly intact, save for a small circular opening the size of the lead in a pencil, which on pressure exuded a pus-like material from it. There was no evidence of old or recent hemorrhage and no thrombosed vessels were observed. Examination of the pus-like material failed to reveal bacteria, and no cells could be found. The material consisted of a fine debris. Above the level of the fifth dorsal segment the cord was intact. Sections made through the tenth dorsal segment of the cord showed a number of necrotic-looking cavities in the posterior and lateral tracts, which contained a soft creamy debris. Sections through the eleventh segment showed a single cavity in the posterior tracts which only extended to about the middle of the segment. Below this level the cord showed no changes.

Microscopic Examination. Sections made from the eighth dorsal segment in the region of the greatest macroscopic change showed an almost complete necrosis of all structures within the cord. The area formerly occupied by the cord was replaced by a debris contained within the pia mater. Along a portion of the pia and apparently adherent to it was a thin layer of nervous tissue, showing much degeneration. This tissue could also be observed along the anterior sulcus where the pia with the bloodvessels was still intact. The central canal was to be seen and its lumen was patent. There was no evidence of a proliferation of the cells lining the central canal. The gray matter of the cord and particularly the anterior horns could be followed in outline, but showed extensive degenerative changes in its structure. A number of pyramidal cells showing chromatolysis were observed. On the other hand, the tissue of the posterior portion of the cord, including the white matter and the posterior horns, was disintegrated. Within these cord lesions there was no evidence of an inflammatory reaction. Leukocytes and lymphocytes were entirely wanting. Moreover, a careful

study of the sections failed to reveal any evidence of thrombosed vessels within the cord. It was observed that in the small portions of the nervous tissue remaining opposite the severely damaged area the glia cells appeared more prominent than normal. These cells were to be observed as large spherical or at times irregularly shaped structures having very few processes. Some of the cells resembled endothelial cells, save that the nucleus was eccentric and occasional ones had short fibers. These cells were more prominent in the white matter than in the remains of the gray. Sections made through the fifth, sixth, and upper part of the seventh segments of the dorsal cord showed a fairly intact structure, save in the presence of a simple cavity lying immediately behind the commissure and slightly to the right side. This cavity occupied the white matter of the cord, and only bordered upon the gray. The tissue of the commissure was not involved, and although the central canal appeared to be narrowed the cells lining it did not enter into the formation of this cavity. The cavity was irregularly outlined and had no lining membrane. A necrotic wall without inflammation was its boundary. The tissue surrounding the cavity was loose and almost edematous. In places the large spherical glia cell was prominent, and although forming small aggregations, did not develop into masses. An irregular reaction in the glia cells of the white matter was to be observed in different portions of the cord. Immediately external to the posterior horns were seen occasional aggregations of large glia cells, which had developed immediately surrounding the bloodvessels. The diameter of the cavity passing upward toward the dorsal cord was not uniform but varied, at times occupying

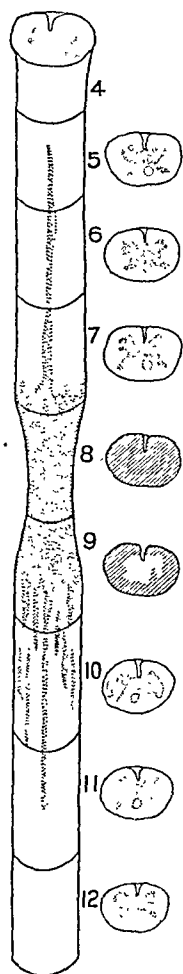


FIG. 1.—Cord of Case I, in which almost complete absorption of the eighth and ninth segment has taken place. A single cavity is seen passing upward, while multiple small cavities pass downward and enter the tenth and eleventh segments.

the entire width of the white matter lying between the posterior horns immediately behind the commissure. A similar but more irregular cavity formation was found in the segments below the level of the main lesions. In the tenth dorsal segment a number of irregular necrotic cavities were found in the white matter of the posterior

columns, as well as in the lateral columns. The character of the cavities was similar, in that none of them had a lining membrane, but were bounded by a loose and partly necrotic tissue. In the eleventh dorsal segment a single cavity was present in the posterior columns. In no section was there any association of the cavity formation and the central canal to be observed. Sections of the dura mater showed a considerable thickening of the outer tissues and the presence of an infiltration by lymphocytes and plasma cells. The bloodvessels in the dura were the seat of an inflammatory reaction, but none of them showed a complete closure of their lumina. In only one vessel, a vein, was there found a recent adherent thrombus which was undergoing organization. The vessels lying immediately around the cord in the pia appeared normal.

Anatomic Diagnosis. Acute softening of the cord; syringomyelia; chronic pachymeningitis; chronic localized empyema of the thorax; interstitial abscess of the thoracic wall; unresolved pneumonia, with abscess of lung; old pleural adhesions; acute suppurative cystitis and pyelonephritis; trophic ulcers of skin.

The patient was suffering from a chronic pyemia and empyema in which the suppurative process of the thorax had extended into the spinal column and over the dura at the eighth dorsal segment. A decided inflammatory reaction was present on the outer surface of the dura, but it did not extend within this membrane. The sudden onset of the paraplegia, with complete loss of sensation, suggested hemorrhage or embolism of the vessels of this part of the cord. The microscopic examination showed no evidence of old or recent hemorrhage, and the lesion, which was the seat of extensive disturbance, consisted of an almost complete liquefaction and absorption of the cord structures at about the eighth dorsal segment. This cord destruction gave no indication of a true myelitis, nor was there evidence of new-growth. From this extensive and severe lesion there extended in both directions of the cord, cavities containing a necrotic material and outlined by irregular walls. One cavity extended upward into the fifth dorsal segment, while another passed downward as far as the eleventh dorsal segment. There was no evidence that the spinal canal was in any way involved or associated with the cavities, nor was there an ependyma lining them. In a number of sections a reaction was observed in the glia cells amounting to a proliferation of this tissue in the vicinity of the cavity formation. In other regions, however, changes in the glia were entirely wanting. The cavity formation involved mainly the white matter of the posterior columns.

CASE II.—J. H., aged twenty-five years; laborer. The patient was admitted to the Mercy Hospital on January 16, 1912, under the service of Dr. G. O. Goulding. On admission the patient complained of the loss of the use of both lower extremities.

Previous History. About two weeks ago he did not feel well and noticed that his legs felt sore. He was able to walk on January 14 and 15, but on January 15, on attempting to get up in the morning, he found he was unable to walk or stand. He had no indication of the onset of this condition. Closer questioning of the patient revealed no detail of the present illness. He denied having had any accident or acute infection in recent years. At the time of admission there was a complete motor and sensory paralysis below the level of a line situated about midway between the nipple and umbilicus. The anesthesia was complete to all forms of sensation. There was no voluntary control of the sphincters or the bladder. As the patient had to be catheterized, and although every care was taken to prevent infection, a cystitis developed about four weeks after admission. Further, large decubitus ulcers developed which were very deep and showed no attempt at repair. The patient gradually became septic, and died three and a half months after the onset of the paralysis.

Clinical Diagnosis. Acute transverse myelitis. Death resulted from sepsis.

Autopsy. An autopsy was performed sixteen hours after death. The body was 161 cm. in length and showed marked emaciation. Over the sacrum and both trochanters there were large ulcerating areas, which extended to the bones, and about 15 cm. of both femurs were exposed. The crest of the left ilium was exposed throughout its whole length. Over the chest and knees small round ulcers were seen.

Brain: The skullcap showed nothing abnormal. The dura was not thickened. The Pacchionian granulations were prominent. The hemispheres were of quite normal appearance on their surfaces. There was no evidence of exudate under the meninges. On opening the brain the ventricles were free from exudate. They were not dilated. The brain substance was a little pinkish, but showed nothing abnormal. The cerebellum was without change.

Cord: On opening the spinal canal no change could be observed about its bony structure or upon the outside of the dura. The dura was of usual thickness and its inner surface was smooth. There was no evidence of exudate upon the meninges. The vessels of the pia were injected along the posterior surface. The entire cord appeared swollen and larger than normal. The pia-arachnoid was tense and appeared to be stretched over the cord. In several places where the pia was slightly torn the cord substance bulged outwardly. The most marked change in the cord was between the seventh and eighth dorsal nerves, where there was an area of extensive softening which extended in both an upward and downward direction. Taking the middle point of the softening as existing between the seventh and eighth dorsal nerve roots, the softening of the cord, which involved the entire structure, extended 3.5 cm.

in both directions, in which no structure could be made out. Smears from this softened material showed debris without the presence of any leukocytes. A greater or less change was to be noted in all portions of the remaining cord. Opposite the fifth dorsal vertebræ the cord structure was altered and showed the presence of a softer and whiter area occupying the posterior horns and all the tissues lying between them. What remained of the cord in this area was congested. At the level of the sixth dorsal a similar whiter and softer area was found, but here it was of greater extent. In this region the right anterior horn was also involved by the presence of new-growth. Similar areas of change were noted in the portion of cord below the softened tumor mass. At the upper extremity of the lumbar enlargement the cord was much congested and its markings indistinct. Here, again, however, the posterior portion of the cord was affected. In the pia, at about the tenth dorsal, was seen a small, flat, calcareous plaque.

Microscopic Examination of the Cord.

Sections of the most involved portion of the cord showed a tissue in which normal cord structure could no longer be discerned. The tissue was composed of a fine reticulum and many irregularly distributed nuclei. In the reticulum there was a fine debris looking like degenerated reticular fibers. The nuclei were round and a little smaller than those of lymphocytes. Ganglion cells could not be found. In this tissue the reticulum appeared looser and almost vacuolated, as if a process of degeneration were present. There was, however, in this main tumor mass no evidence of cavity formation. This tissue occupied the entire cord at the level of the eighth segment. In the lower portion of the ninth segment a similar reticular tissue occupied the posterior columns and to a certain extent the lateral tracts. The gray matter was also encroached upon and its outline irregular. What remained of the white matter of the cord was much vacuolated and loose. The tissue occupying the area

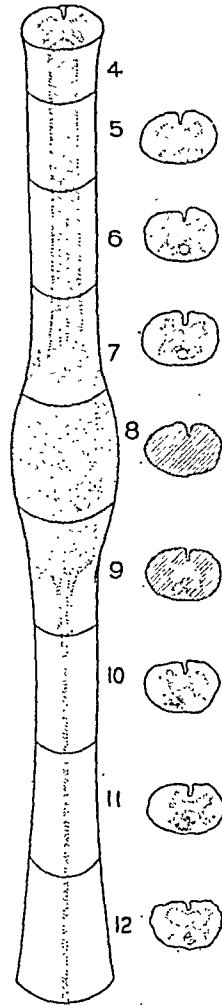


FIG. 2.—Cord of Case II, showing a gliomatous mass occupying the eighth and a part of the seventh and ninth dorsal segments. From this tumor a linear tumor mass passes upward and downward in the posterior columns. Within this extension of the tumor is found a process of cavitation.

between the posterior horns showed evidence of degeneration and necrosis. Thus a mass of necrosis lay within the new-growth occupying the posterior columns. The new-growth could be followed through the succeeding segments of the cord down to its extremity, and within this area an irregular cavity of varying dimensions was present. In the lowermost segment of the cord the cavity was quite patent without the presence of the necrotic island observed elsewhere. The distribution of the tumor mass in the lower cord varied at different levels, but the main portion was found to occupy the posterior columns. The gray matter was variously involved. In the portion of the cord above the main tumor the invading glial tissue had followed the posterior columns. In places, however, other tracts were also invaded, but without any regularity. The invading tumor consisted of a loose reticular structure in which masses with more closely aggregated nuclei were observed. The tissue appeared quite vacuolated. This appearance was more apparent than real, in that many of the tumor cells were composed of large spherical cells with finely granular protoplasm. The reticulum consisted of fine threads associated with smaller cells with dark-staining nuclei. The tissue of the new-growth was quite vascular. The central canal showed a close aggregation of its nuclei and an apparent closure of its lumen. Opposite the eighth dorsal segment some tumor mass was also found in front of the right anterior horns. Extending through the tumor mass and always lying posterior to the commissure was a cavity which began in the seventh dorsal region and extended as high as the lower border of the fifth segment. This cavity had an irregular outline, with necrotic borders. Tumor tissue formed its outer boundary. There was no limiting membrane and tissue debris was found within. The bloodvessels in the vicinity of the tumor or of the cavity showed no evidence of thrombosis and no particular change was to be noted in the vessel walls. In some instances the coats of the small arteries appeared somewhat loose. New bloodvessels with thin walls were evident in the new-growth. In the sixth dorsal segment was found a small cavity isolated from the previously mentioned posterior channel, and apparently having no connection with other openings. This cavity formed an isolated area of degeneration in a small tumor mass, lying in the lateral tracts. The tumor which extended along the posterior columns was more extensive and far-reaching than the cavity formation.

Anatomic Diagnosis. Glioma of the cord with softening; syringomyelia; acute suppurative cystitis; pyelonephritis.

In the second case we are dealing with a man who previous to the onset of the present condition suffered no ill health or accident which might be associated with the lesion in the cord. Without any warning he suddenly found himself completely paralyzed

from the waist down. The paralysis was permanent, and with it extensive trophic ulcers as well as sepsis, beginning in the urinary tract, led to his death some months later.

At autopsy a complete transverse destruction of the cord due to the invasion of a soft glioma was found. This new-growth not only occupied the original diameter of the cord, but even led to a tissue mass considerably greater than the diameter of the cord. This new-growth was situated at the eighth dorsal segment, and from this region the new-growth extended both upward and downward along the posterior tracts. It was in this new-growth that cavities developed by a process of degeneration.

In comparing our two cases it is evident that the cavity formation in the one is entirely different in origin from the other. In each instance, however, it is evident that the development of the cavity had been the result of a necrotic process and that the presence of the channels had in no way been related to the structures forming the central canal. In each instance the wall forming the cavity was ragged and formed by degenerated nervous tissue.

Moreover, no evidence could be found that hemorrhage played any part in the formation of these cavities. In fact, in neither case was there old or recent hemorrhage present.

The question which is of greatest interest concerns the way in which progressive cavity formation may take place in the cord. In considering the cases immediately under discussion we need hardly consider the question of syringomyelia occurring from anomalies of development. Such cases have been discussed by Virchow, and later enlarged upon by Seiden. It is of interest, however, that these authors believed that at times congenital cavities of the cord were followed by hemorrhage and softening as well as new development of glial tissue which would make them simulate the acquired types of the disease. It would, however, be preferable to retain the term hydromyelia for those cases in which the cavity had a development associated with the central canal.

Langhans offered an explanation for those cases in which the central canal alone was dilated. He believed that the process was the result of blood stasis in the posterior part of the skull which led to a venous hyperemia of the cord. The condition therefore simulated a transudate due to passive congestion. Under some conditions the process might later develop into a diverticulum.

The same view was held by Kronthal, who, however, indicated that the condition of passive hyperemia occurred in connection with processes within the spinal column as tumors, chronic meningitis, meningeal adhesions, or compression of the spinal cord. In general the theory of hyperemia found few supporters. Others have indicated that there was a relation between inflammatory thickening of the meninges and the development of cavities in the cord. Thus cases of acute cerebrospinal meningitis, with subse-

quent syringomyelia, are described (Saxer), while Phillips and Oberthur brought forward evidence showing the simultaneous development of thickening of the dura and cavitation of the cord. In many of the reported cases of syringomyelia there was an associated spinal pachymeningitis, but its direct etiologic bearing on the cord condition is far from clear. In our first case a similar association was present, but here the pachymeningitis was clearly the result of an external inflammatory process, while the leptomeninges were not involved. The association of two conditions appears in this case coincident and not directly related. Moreover, autopsies not uncommonly reveal pachymeningitis, adhesions of the membranes, and various lesions of the cord without the process of spinal cavitation.

In those cases of hydromyelia in which the condition is one of dilatation of the central canal there is evidence of a secondary compression and atrophy of the surrounding nerve structures. In the majority of cases of syringomyelia symptoms of this character are entirely wanting.

According to Joffroy and Achard, syringomyelia bears no relation to hydromyelia nor to conditions arising from the central canal. They believe that it arises from chronic inflammatory processes in the gray matter of the cord, which later give rise to cavity formation. The destruction of tissue is particularly associated with circulatory disturbances, probably thrombosis.

The most widely accepted theory of the process is that of Simon and Schultze, which indicates a primary growth of the ependymal and peri-ependymal tissues of the character of gliosis. This development of new tissue progresses along the cord, while a necrosis with subsequent cavity formation develops in the inner and older portion of the growth until the true nature of the tissue can only be observed in the peripheral and distal portions. In some places the nature of the growth indicates a true glioma, and Weigert believes that a differentiation can be made between gliosis and glioma. Occasionally a communication may develop between the cavities of the new-growth and the central canal.

A number of cases of gliosis without the presence of tumor in the posterior columns of the cord have been described. Oppenheim discussed a case under the name of gliosis spinalis in which the symptoms had been those of tabes. The process extended from the cervical to the lumbar cord and occupied mainly the posterior portion of the gray matter. Here and there this tissue contained small lumina.

Against the contention that tumor development always precedes the formation of the new cavity in the spinal cord, Gerlach indicated that some cases showed no evidence of enlargement of the cord as we would expect from tumor, nor did the cord show the usual areas of softening as is seen about gliomas. The irregular

position of the cavity as it occurs in different cases does not permit a common theory of origin.

However, it cannot be denied that in some instances the cavity formation was preceded by true tumor of the nature of glioma. This has been the condition in our second case. Thus we find the undoubted presence of a localized glioma which has increased the diameter of the cord and which in its oldest part has undergone softening. In the main tumor a cavity cannot be distinguished, and the whole mass is so soft that it cannot be handled without producing artefacts. In the further extension of the tumor, central liquefaction with partial absorption has given rise to cavity formation. Thus we have a well-marked glial tumor with secondary cavitation. But, on the other hand, there are cases in which the development of the cavity precedes a glial proliferation, while in a certain group of cases it is impossible to say from the nature of the tissue whether we are dealing with a glioma with extensive cavitation or with a primary syringomyelia having a considerable secondary gliosis.

Within the true tumors the thin-walled bloodvessels are prone to give rise to hemorrhage. At other times the vessels in and about the tumor undergo degeneration, with partial occlusion of their lumina. In these cases central necrosis of the tumor, with cavity formation, is not uncommon. It has been indicated by some that in the early stages of such tumor development, and before definite symptoms have arisen, there is a considerable chance of hemorrhage from trauma which otherwise would have been without harm.

Instances in which cavity formation had occurred subsequent to traumatic hemorrhage within a tumor have also been described.

On the other hand it is evident that cavity formation develops in the cord unassociated with tumor and apparently arising from varied processes. Thus it has been indicated that through primary hemorrhages, cystic cavities may develop, and that a not important cause for the long narrow channels is a progressive necrosis resulting from local vascular or circulatory disease (Westphal).

Thus we find that cavities may be present in the spinal cord under different conditions. These different forms are to be distinguished from each other as having a different mode of origin:

1. *Neuro-epithelioma Gliomatosis*. This is a true tumor having its origin in the cells lining the central canal. The tissue of the tumor is composed of glial cells with a fairly dense reticulum in which are distributed gland-like elements with lumina of different sizes (Rolly, Schultze, Kahler, Schlesinger, Ribbert, and Wright). Babes has indicated that the cells of the central canal sometimes show an inherent tendency to proliferate, giving rise to the ependymal adenomas. Hutchinson suggests that his second case, in which only a small cavity with an epithelial lining was found, had

its origin in some misplaced ependymal cells which under certain vascular stimuli had developed into a cystic cavity.

2. *Diverticula of Central Canal.* A number of cases have been described in which an accessory canal communicating with the central canal of the cord has been found. These accessory channels are lined with the ependymal cells continuous with those in the central canal. The process is probably a congenital anomaly of defective closure (Jacoby and Kahler).

3. *Anomalies of Closure of the Posterior Sulcus.* At times a channel has been observed lying posterior to the commissure and having its walls composed of connective tissue. Some of these channels have been found to communicate with the surface, and it has been indicated that they result from an improper closure of the posterior sulcus in which some of the external membranes have been included (Jacoby, Gerlach). Thomas and Hauser's case probably belongs to this class.

4. *Degeneration of Gliomas.* The greatest number of cases of syringomyelia have probably been described under this class. It has usually been considered that the formation of a cavity within gliomatous tumors has been the result of necrosis from inadequate nutrition or of hemorrhage into the tumor, with subsequent absorption. Such cavities have a necrotic border of tumor tissue without a definite limiting membrane to the cyst. These tumors advance either along the gray matter or along the nerve tracts of the cord. This longitudinal growth may be rapid and the process of cavity formation within the tumor follow closely upon the development of the new-growth. Hyaline and other changes have been described in the walls of the bloodvessels of the tumor, and it has been assumed that these are predisposing factors for subsequent necrosis or hemorrhage.

5. *Primary Syringomyelia.* This class is a comparatively small one and includes those cases in which the cavity formation preceded a gliosis in the cord. In some instances the amount of change in the glial tissue was comparatively slight, while in others regenerative changes were extensive throughout the cord. The processes leading up to the formation of such cavities within the cord are various. Hemorrhage from trauma or spinal apoplexy (Kienboch, Brasch, Westphal, Spiller, and others), thrombosis or embolism of the spinal arteries (Chiari), venous and lymphatic stasis, acute toxic degenerations, changes in the spinal meninges (Japha, Oppenheim), leprosy (Dyer), an occlusion of the spinal canal have each been described as causative factors. As, however, the condition primarily bringing about the lesion in the cord does not lead to the death of the patient, the time that intervenes from the onset of the condition to the death of the patient permits of such further pathologic changes in the cord that a definite statement as to the initial cause of the lesion is often difficult to make. Thus, for

instance, in our first case the clear-cut history would point to embolism or thrombosis of the vessels of the eighth dorsal segment (hemorrhage of the cord having been ruled out by the microscopic findings), and yet there is no positive microscopic evidence to establish the proof. The extensive softening occurring in the cord at the site of primary damage had also destroyed the contained vessels.

An examination of the tissues of this case also indicates that the cavity in the cord became progressively larger and that it continued to extend longitudinally. In other words the entire cavity did not develop at one and the same time. Why, by a process of necrosis and without the presence of an infiltrating tumor, such a cavity should continue to extend through the length of the cord has not been fully explained. It would appear that the process is intimately associated with the blood supply and the vascular anastomosis. In those cases where the spinal arteries have been occluded by embolism or thrombosis it is probable that thrombi continue to extend into the smaller branches and anastomoses of a particular region of the cord, and depending on the extent of the vessels involved, there develops a progressive necrosis with cavity formation.

The reaction occurring in the glial tissue in these cases of primary syringomyelia resembles an irritative hyperplasia. The irritant, probably the products of tissue degeneration, is too slight to lead to an inflammatory reaction, while, however, the cells of the immediate neighborhood respond in proliferation. Similar reactions in the glia are to be observed in the vicinity of cerebral hemorrhages.

BIBLIOGRAPHY.

- Baumler. Inaugural Dissert., Leipzig, 1887.
 Bawli. Inaugural Dissert., Königsberg, 1896.
 Chiari. Zeitschr. f. Heilkunde, vol. ix.
 Gerlach. Deutsch. Zeitschr. f. Nervenheil., 1886, iv, 271.
 Holmes and Kennedy. Brain, 1909, xxxi, 493.
 Hutchinson. Bull. Ayer Clin. Lab., 1906, i, 63.
 Joffroy and Achard. Arch. de Méd. Expér. et d'anat. et Path., 1895, No. 1.
 Krontal. Neurologische Centralbl., 1889, viii, 574.
 Kahler. Arch. f. Psychiat., 1880, x, 179.
 Langhans. Virchow's Archiv, 1881, lxxxv, 1.
 Lehmann. Inaugural Dissert., Jena, 1907.
 Müller. Inaugural Dissert., Jena, 1896.
 Oppenheim. Arch. f. Psych., 1893, xxv, 315.
 Rolly. Deutsch. Zeitschr. f. Nervenheil., 1902, xxi, 355.
 Saxer. Beitrag. z. path. Anat., 1902, xxxii, 276.
 Schlesinger. Die Syringomyelie, Leipzig, 1902.
 Schultz. Virchow's Archiv, 1882, lxxxvii, 510.
 Spiller. AMER. JOUR. MED. SCI., 1896.
 Schmaus and Sacki. Lubarsch-Ostertag's Ergebnisse, 1900, v, 320.
 Simon. Arch. f. Psych., 1875, v, 132.
 Van Gieson. Proc. New York Path. Soc., 1891, p. 72.
 Wright. Jour. Exper. Med., 1910, xii, 550.
 Westphal. Arch. f. Psychiatrie, 1902, xxxvi, Heft 3.
 Weigert. Cent. f. alleg. Path., 1889, i, 729.

MODERN GENITO-URINARY DIAGNOSIS AND TREATMENT, WITH REFERENCE ESPECIALLY TO LABORATORY METHODS.¹

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THE scope of the subject of this article is so extensive as to make its complete portrayal, in any form other than a book, an impossibility. Consequently, I shall be content to discuss, in a cursory manner, merely the more important advances, diagnostically and therapeutically, that have marked the progress, in recent years, of genito-urinary surgery from the laboratory and endoscopic standpoints. In order to systematize my remarks, the urogenital system will be considered in turn under its anatomic parts—the urethra, the prostate and seminal vesicles, the vasa deferentia, epididymites and testicles, the bladder, the ureters, and the kidneys, with an appendix delegated to syphilis.

THE URETHRA. Irrespective of the value incident to the routine bacteriologic and cytologic examination of every urethral discharge, it should be a fundamental law, with imperative obligation on the part of each clinician, to investigate immediately, definitely, and precisely the source of any urethral discharge, whether blood or pus, not known absolutely to originate from the urethra. From this obvious professional duty any digression is not only inexcusable but decidedly reprehensible. Those incipient cases of renal tuberculosis, neoplasm, and vesical papilloma which Nature has provided with that initial distress signal, the red blood corpuscle, and which are treated lightly by the administration of a urinary antiseptic under the guise of that too frequent diagnosis and very rare condition, essential hematuria, for a few weeks or months, during which period the lesion not uncommonly progresses to the inoperable state, are observations and experiences unfortunately too well known to us all.

Glass Tests. The time-honored two-glass and three-glass tests, Kollmann's five-glass test, and Young's seven-glass test not infrequently subserve a useful purpose in clinical urinalysis, but it must be remembered that any "glass test" is fallible and commonly leads to inaccurate diagnosis. Nevertheless, routinely, they are of considerable practical utility, with proper interpretation.

I wish particularly to invite attention to a *seven-glass test* which will prove of value in the differential diagnosis of the origin of

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urogenital pyuria and hematuria, especially as a temporary procedure in the absence of those more exact instruments, the cystoscope and urethroscope. The test is performed as follows:

1. The anterior urethra is thoroughly washed out with normal salt solution or distilled water, employing the common glass dressing or piston syringe, or a catheter of medium size. This washing constitutes glass No. 1.

2. Glass No. 2 is a continuation of this irrigation, and serves as a control to prove whether or not the first washing was complete.

3. Glass No. 3 is a partial voluntary urination by the patient, and contains any pus, blood, or exudate originating from the posterior urethra, its appendages, and the higher urologic system.

4. Glass No. 4 is a continuation of No. 3 and serves as a control of its predecessor. It contains only that part of any posterior urethral contamination which may have leaked back into the bladder or originated from the bladder and kidneys; if the posterior urethral exudate is scanty and the higher urinary tract is normal the urine will appear clear.

5. Glass No. 5 contains that portion of urine voided after massage of the prostate and seminal vesicles, and serves to determine the condition of these organs.

6. Glass No. 6 is a continuation of No. 5 and serves as a control of the same, in order to determine whether or not the posterior urethra has been thoroughly cleansed of the secretion and exudate expressed from the prostate and seminal vesicles.

7. Glass No. 7 contains the final urination and indicates the character of urine contaminated by any lesion of the upper urinary tract, as the bladder or kidneys. Glasses Nos. 6 and 7 both may contain material expressed at the time of prostatic massage which has leaked back into the bladder. Comparison, however, with No. 4 will readily reveal the true nature of the vesical urine.

Thus observance of the seven glasses may permit of the following deductions:

Anterior urethritis=exudate in glass No. 1.

Posterior urethritis=exudate in glass No. 3, or glasses Nos. 3, 4, 5, 6, and 7; if in the latter series, it is most marked in No. 3.

Prostatitis or prostatitis and seminal vesiculitis=exudate in glasses No. 3 or 5, or Nos. 5, 6, and 7; in any event it is most conspicuous in No. 5.

Cystitis=exudate evenly distributed in glasses Nos. 3, 4, 5, 6, and 7.

Ureteritis and nephritis=exudate evenly distributed in glasses Nos. 3, 4, 5, 6, and 7, or most marked in No. 7.

In discussing the glass tests a word of caution must be dropped relative to the inaccuracy of that most frequently employed of all, the two-glass test. The urethroscope has demonstrated that

in chronic urethritis the apparent information thus yielded is invariably erroneous; the second glass is seldom pussy or shreddy, unless the posterior urethral exudate is sufficiently profuse to leak back into the bladder.

Diagnosis and Treatment of Gonorrheal Affections. The differential diagnosis between gonorrheal and non-gonorrheal inflammation of the urethra rests ultimately upon bacteriologic study. No longer does the demonstration of an intracellular, Gram-negative diplococcus substantiate the diagnosis of gonorrhea. Indeed, in medical jurisprudence and the courts of justice today, in order to render the evidence legal, the gonococcus must be culturable. Irrespective of the law of the land, bacteriologically, if the identification of the Neisserian diplococcus depended upon its culturability there would exist few cases capable of the diagnosis of gonorrhea. The culture medium which we have found best adapted for the growth of the gonococcus is one prepared from the formula of Dr. John C. Torrey. It consists of the addition of one part of rich ascitic fluid to three parts of meat-infusion peptone agar with 2 per cent. glucose, after the latter has been titrated to about +0.8 to phenolphthalein. Again, the differentiation between the *Diplococcus gonorrhœæ* and *Micrococcus catarrhalis* by stained smear is an impossibility; both are Gram-negative and morphologically identical. Culturally the distinction is readily determinable.

Eosin-azur Stain. It has been pointed out that even the Gram-differential stain may fail in the identification of the gonococcus. Routinely many simple stains have been and are utilized for the demonstration, practically, of the diplococcus of Neisser. I wish to call attention to one which in my opinion is most meritorious: One tablet of the commercial eosin-azur is dissolved in 5 c.c. of pure methyl alcohol. A thin film coverslip smear of the suspected material is prepared and dried in the air. A given number of drops of the stain, sufficient to cover the smear, are placed on the coverslip for one to two minutes; to these are added twice the number of drops of distilled water and the whole permitted to stand five additional minutes. The coverslip is then passed through the distilled water, dried, and mounted. The stain is differential to the degree that the gonococci appear as dark blue bodies, the nuclei of the leukocytes as a purple, while the protoplasm assumes a faint blue color. Thus the gonococci are very conspicuous and readily distinguished.

Gonococcus Complement-fixation Test. Schwartz and McNeil continue to assert the increasing value of the complement-fixation test for the diagnosis of gonorrheal infections. They assert that a positive reaction denotes the presence or recent activity in the body of a gonorrheal focus; a negative reaction, however, does not exclude gonococcal infection. A positive reaction is not obtained if the disease is limited to the anterior urethra, nor is it to be ex-

pected earlier than the fourth week, and then only in the event of an acute infection or complication. A positive reaction may persist seven or eight weeks after the pronouncement of cure, and means that the patient should be regarded as still harboring gonococci. About 30 per cent. of cases, clinically considered as post-gonorrheal, demonstrate a positive reaction. Approximately 55 per cent. of patients suffering from chronic prostatitis within three years of the gonorrheal infection give positive reactions. About 13 per cent. of patients supposedly clinically cured for a period of three months exhibit a positive reaction. In women positive reactions are rarely obtained unless the cervix has been involved. In the future it seems logical to infer that more may be expected of this test gynecologically, and also relative to cure and the matrimonial fitness of candidates.

Bacterins and Sera. Although the employment of Neisserian bacterin in gonorrhea seems to be more or less definitely limited, I have repeatedly been able to diagnose correctly a synovitis or arthritis, indefinite as to etiology, by the hypodermic administration of large-sized doses of gonococcus bacterin, eliciting thereby a local reaction, analogous to the tuberculin test for tuberculosis. Therapeutically in acute chronic gonorrheal urethritis and in the common complications other than synovitis and arthritis the bacterin has proved of little or no value, although we are as yet unprepared to express final opinion as to its possible value in lessening stricture formation. On the other hand, in joint complications and vulvovaginitis of children, it has been signally meritorious. It is generally acknowledged that gonococcus bacterin has been a failure in the treatment of prostatitis, seminal vesiculitis, and epididymitis. I believe the explanation of this is apparent in the fact that these complications are almost invariably the result of superimposed mixed infection. Naturally a gonococcus antigen will be futile against infections due to the *Micrococcus albus*, *candicans*, or *catarrhalis*, the *Streptococcus pyogenes*, the colon bacillus, etc. On the contrary, I have been convinced many times that the preparation and administration of an autogenous bacterin, as an accessory therapeutic agent, has materially shortened the convalescence in these patients.

Antigonococcic serum prepared in accordance with the work of Rogers and Torrey for the treatment of synovitis or arthritis and systemic gonorrheal involvement is unquestionably the remedy *par excellence*, superseding in promptness and effectiveness Neisser bacterin. The initial dose should be from 2 to 4 c.c. injected subcutaneously on the peripheral side of the joint.

With respect to bacterins and sera it must be emphatically stated that there are no agents in modern therapeutics more abused than these biologic products. At all times it must be remembered that with careless or improper administration they may be more

potent for evil than for good. Finally they are to be regarded simply as accessories to Nature, not "cure-alls."

Urethroscopy. Mechanical improvements during the past few years in the construction of urethrosopes and cysto-urethrosopes have materially enhanced the utility of these instruments both for purposes of diagnosis and treatment. By their employment anterior and posterior urethritides are accurately differentiated, granular patches located for topical applications of silver nitrate, papillomas diagnosed and destroyed by the high-frequency current, disease of the veru montanum precisely studied, cysts and papillomas of the internal vesical sphincter defined and treated, infections of Littre's glands and para-urethral abscesses discovered, incised and evacuated by direct endoscopy, the orifices of fistulas and false passages definitely located, and finally protruding median prostatic lobes and bars excised or punched out.

THE PROSTATE AND SEMINAL VESICLES. *Bacteriological Examination.* For the sake of convenience, and because often it is impossible to examine one without molesting the other, these organs will be considered together. Inflammation, whether parenchymatous or interstitial, circumscribed or diffuse, is the commonest of all diseases to which they are subject. As a rule the clinical symptomatology in conjunction with rectal palpation suffices to establish the diagnosis of prostatitis. There are, however, countless cases in which the microscopic examination alone of the secretion and exudate, expressed by massage, will demonstrate the presence or absence of inflammatory disease. Frequently it is found that a markedly cloudy urine filled with flocculent material of a dirty grayish color upon microscopic examination consists exclusively of normal spermatic fluid. On the other hand an opalescent urine, after prostatic massage, evidencing, microscopically, a normal state often reveals by the microscope quantities of pus cells. The practice is universal, yet how many physicians resort to the microscope together with prostatic massage before discharging their patients with gonorrheal urethritis?

The microscope in addition to the demonstration of pus may reveal the presence of bacteria as the gonococcus, the tubercle bacillus, and other pyogenic organisms. Should it fail the exudate may be, and under certain conditions must be, cultured. If tuberculosis is the suppository possibility the suspected material should be injected into guinea-pigs by the Block and intraperitoneal methods.

Since the bacteriologic and immunologic side of this subject must be considered in greater detail in the discussion I have only to remark that it has been my experience that much may be expected from the proper employment of autogenous bacterins in many cases of suppurative prostatitis and seminal vesiculitis.

Microscopy. Finally the microscope is of paramount importance in the examination of spermatic fluid to determine its normal or abnormal character, the presence and viability of spermatozoa, with respect to sterility and the identification of the characteristic dark brown crystals by the use of Florence's reagent in certain medico-legal problems.

Cysto-urethroscopy. It is generally recognized that the sago or tapioca bodies commonly seen in the urine after prostatic massage have their origin from the seminal vesicles. Occasionally these characteristic masses are dirty gray or brownish in color, incident to inflammation of the vesicles. The diagnosis may then be confirmed by the microscope, or if the expressed material is purulent, posterior urethroscopy will frequently reveal pus casts exuding from the ejaculatory ducts or an exudate filling the utriculus.

The cystoscope or, better, the cysto-urethroscope serves, furthermore, a not unimportant sphere of usefulness with respect to the prostate. Its value in the diagnosis of the character and degree of intravesical enlargement of this gland is too well known to require comment at this time; its value in the determination of associated bladder conditions as calculus and tumor, the relative enlargement of the lateral and median lobes, or the mere presence of a median bar or valvular lobe obstructing the internal vesical sphincter, are considerations inducing the twentieth century genito-urinary surgeon to think twice before adopting the perineal, suprapubic, or endo-urethral procedure of prostatectomy.

THE VASA DEFERENTIA, EPIDIDYMITES, AND TESTICLES. *Bacteriology and Serology.* Although certain bacteria, notably the *Bacillus tuberculosis*, may be identified from the urine voided per urethram, in the case of disease of the vas, epididymis, or testicle, laboratory methods other than the histopathologic have little to offer with respect to the diagnosis and treatment of affections of these organs. I shall allude merely to the value of the Wassermann reaction, to be discussed later, and the employment, diagnostically and therapeutically, of tuberculin.

Tuberculin. With respect to the use of tuberculin, diagnostically, I desire to state that not only here, but generally, I have never been misled by the disclosures of this test. With the possible exception of children and patients with a temperature over 100° F., or in the last stages of disease, the subcutaneous method is unquestionably the least fallible. In children and certain febrile cases the von Pirquet method may be more desirable. I have found Old Tuberculin the preferable preparation for the purpose, and administer as an initial dose 0.5 mgrm., increased if necessary in a series of four inoculations to 5 mgrms. Too much stress cannot be imposed on the fact that a positive reaction depends upon both a general (rise of 1° in temperature) and a local response for the diagnosis of a suspected local tuberculosis. I have seen cases of

epididymitis following gonorrhea in which the current etiologic bacterium was impossible of determination, correctly diagnosed by the use of tuberculin and subsequently markedly benefited by the administration, therapeutically, of the Bacillen Emulsion preparation.

THE BLADDER. The bladder may properly be regarded as the bureau of information for tuberculosis of the urogenital system. It is undoubtedly well recognized that the tubercle bacillus may invade the bladder from contiguous disease of the prostate, seminal vesicles, and even from the epididymis and testicle; but it is unquestionably too little recognized that one of the most important, frequent, and often earliest symptoms of renal tuberculosis is vesical irritability.

Bacteriologic Examination of Urine. The differentiation of tuberculosis from other pyogenic infections of the bladder is readily possible, microscopically, culturally, or by animal inoculation; and the determination as to the primary or secondary site, and if the latter, as is almost invariably the case, of the original focus of the disease, is usually promptly disclosed by cystoscopy, with or without ureteral catheterization and bacteriologic examination of the collected urine.

Although the dictum of Rovsing that pyuria in the absence of the common pathogenic bacteria means tuberculosis, which fact may readily be established by the microscope and cultural procedures, the absolute and final diagnosis depends upon animal inoculation with the sediment from a twenty-four-hour specimen of urine. Two methods are in vogue. The older intraperitoneal injection of guinea-pigs has been largely superseded by the Block or inguinal subcutaneous method, by which technique the findings seem to be just as accurate and the time of determination of the result shortened from three to six weeks to seven to ten days.

The Cystoscope. The invention that has accomplished most for the advancement of urology and has succeeded through its modern perfection in elevating genito-urinary diagnosis and treatment to a plane second to none in surgery is the cystoscope. Indeed in no system in the human organism is diagnosis possible with equal exactitude.

The types of the cystoscope are manifold. Briefly they may be classified according to purpose, as simple examining, ureteral catheterizing and operative, including both the vesical and urethral or cysto-urethroscope; in accordance with construction, as simple tubular and lens and prism system, including the direct and indirect types with or without corrected image, embodying the right angle, oblique forward and retrograde vision; and finally with respect to manner of employment, whether with air or water distention of the bladder. Each cystoscopist will have the greatest satisfaction and obtain the best results with that type of instru-

ment with which he is most familiar. All things being equal, however, it is my belief that the instrument *par excellence* both for patient and doctor is the water cystoscope, constructed on the evacuation-irrigation principle with the indirect vision lens and prism system

Respecting treatment of certain definite vesical conditions the cystoscope today plays an important role. Cauterization and snaring of endovesical growths, as papillomas, have been practised successfully ever since their first performance by Nitze.

High-frequency Desiccation. During the past two years the application of the Oudin high-frequency current promises to eclipse the older endovesical methods, which are open to the same objection as incisional treatment—namely, that often they invite metastasis or recurrence. Even though recurrence may occur following high-frequency coagulation or desiccation, erroneously styled fulguration, the patient is amenable to a repetition of similar treatment, a procedure seldom tenable with the scalpel; moreover, the organic condition of the patient may forbid general narcosis. The technique requires no special instrument other than a high-frequency machine, the electrodes used consisting simply of insulated wires, manipulated through the ordinary ureteral catheterizing cystoscope.

The Lithotrite, the Cystoscope, and the Rongeur. Litholapaxy as devised by Bigelow was intended to and successfully superseded lithotrity. Today no litholapaxy should be considered complete unless supplemented by cystoscopy to determine the total removal of all calculous fragments. Instruments have been devised combining lithotrite with cystoscope, but they have not yet reached perfection. However, I have found the cystoscopic rongeur of Young of considerable value. By its use calculi protruding from the ureteral orifice, stones free in the bladder, and not over 1 c.c. in diameter, and certain foreign bodies are removed through the male urethra. The blades are not powerful enough to crush any save very soft calculi.

THE URETERS. *Ureteral Catheterization.* Primary disease of the ureter rarely occurs. Usually the lesion, whether infection, dilatation, angulation, or stone, is secondary to some renal, vesical, urethral, or extra-ureteral condition. Nevertheless the ureter becomes the object of certain mechanical procedures, either because of its own disease or that of the associated kidney. Most notable among these is ureteral catheterization. It has many indications: (1) to determine the patency of the canal or the nature of obstruction whether stone, stricture, or extra-ureteral pressure; (2) for the collection of urine directly from the kidney for bacteriologic, cytologic, and other examinations, in the differentiation of renal from other disease lower in the urologic tract and for the determination of unilateral or bilateral affections; (3) for the purpose of

lavage of the renal pelvis; (4) for the introduction of radiographic catheters or bougies in the determination of the position of the ureter relative to the x -ray shadows of calculi, calcified lymph nodes, phleboliths, etc.; (5) for the purpose of collargol and other silver preparation injections, in order to skiagraph the dilated, kinked, or misplaced ureters; (6) for pyelography.

Skiagraphy, the Wax-tipped and Dilating Catheter. In addition to the x -ray, unquestionably the best and most reliable procedure in the hands of the expert skiagrapher for the diagnosis of ureteral calculus, there have been advocated a number of devices, employing the cystoscope, for the detection of stone in the ureter. The best of these is the wax-tipped ureteral catheter or bougie. If the calculus is not too large it may be released and its extrusion facilitated by the passage of the Garceau or dilating catheter and the instillation of a few cubic centimeters of sterile olive oil above and below the stone. This procedure should always be adopted before resorting to radical operation if the calculus is of small size and lodged in the pelvic or vesical portions of the ureter.

Tuberculosis. Tuberculosis of the ureter is almost invariably secondary to tuberculosis of the kidney. The ureter commonly becomes partially or completely strictured or occluded, resulting in the so-called "closed tuberculous kidney." In such cases I have twice observed the urine to be free of either pus or tubercle bacilli and the patient afebrile. Under such circumstances, catheterization of the healthy ureter, if attempted, to rule out the presence of infection of the supposedly normal side, may be done without danger of inflicting infection upon the normal kidney. On the contrary, what should be the *modus operandi*, when it is desired to ascertain the integrity of the presumably healthy kidney, when a closed tuberculosis of the other side does not exist and when the bladder obviously contains tubercle bacilli? I well recognize that some surgeons proceed to catheterize, with impunity, for purposes of urinalysis, supposedly normal ureters under these conditions. I feel that such a practice is highly condemnable, in that there is at least the theoretical possibility, by so doing, of infecting the normal ureter and kidney; furthermore, the excretion of tubercle bacilli in the urine is not a uniform process, rendering it necessary to examine twenty-four-hour specimens; hence they might not be found at the time of ureteral catheterization; and finally the demonstration of bacilli tuberculosis in the urine under these conditions does not mean necessarily surgical disease of that kidney, since the renal parenchyma will permit of the passage of tubercle bacilli as well as other bacteria without sustaining permanent disease therefrom. Indeed, it is not improbable that the catheter thus introduced may convey infection from the bladder into the ureter, and the urine per catheter thereby contain tubercle bacilli. Therefore, I believe it to be the saner and wiser

doctrine to discountenance ureteral catheterization in the presence of vesical tuberculosis until its advocates may prove the harmlessness of the procedure. In the meantime a knowledge of endovesical living pathology, particularly with reference to the character of the ureteral orifice, in conjunction with some functional kidney test, as indigocarmin, which is not dependent upon catheterization of the ureters for its performance, will suffice for the practical considerations involved in this question. Certainly, I should not permit the practice upon myself, and I have always found that the rule of self is a fine thing to apply to others.

THE KIDNEYS. The various organic and inorganic constituents of the urine must be passed over without consideration, other than to remark that both albumin and casts may be absent in nephritis, while on the other hand their presence is not necessarily indicative of primary renal disease.

Bacterin and Tuberculin Therapy. I have already alluded to the necessity of ureteral catheterization in the case of the common pyogenic infections of the kidney in order to isolate bacteriologically the etiologic organism. Thus experience has shown that certain conditions, as pyelitis, with or without cystitis, and pyonephrosis have presumably been cured with autogenous bacterins, always however, in conjunction with other well-recognized measures of merit. Again, tuberculin must be given credit for usefulness not only diagnostically, but also therapeutically in tuberculosis of the kidney. The indications for its therapeutic employment should be (1) in the earliest stage of incipency when there is little else other than an indefinite bacilluria with both kidneys functionally sufficient; and (2) in the inoperable stage of bilateral involvement, both kidneys usually presenting insufficiency. In the latter instance I have seen it perform the incredible.

Functional Kidney Tests. The untold number of tests that have been launched from time to time to determine the functional ability of the kidneys is sufficient to prove that none has been found ideal or infallible. It is self-evident that greater reliance can be placed upon two or more tests than upon a single one. They should all be employed in conjunction with the physical, chemical, microscopic, and bacteriological examination of the urine. Those most commonly in vogue, are indigocarmin, phenolsulphonephthalein, the artificial polyuria test, the determination of urea, and cryoscopy of the blood and urine. All with the exception of the first are dependent upon synchronous bilateral ureteral catheterization for the estimation of unilateral function. Thus in the exceptional case where catheterization of the ureter is an impossibility, chromoureteroscopy with indigocarmin has rendered signal service, placing it in the foremost position as the most practical, hence the best, functional kidney test for the purpose of the surgeon. The technique of the test is extremely simple and has been detailed

by the author elsewhere. Suffice it to say that in over two hundred chromoureteroscopies I have found the test well-nigh infallible.

In deference to the phenolsulphonephthalein method it must be conceded that it is a valuable addition to modern urology, and if merely the combined kidney function is desired it may be deserving of first choice, though no more accurate than the indigocarmin test properly performed and interpreted.

Pyelography. The most important recent advance in urology has been the x-ray demonstration of many kidney lesions following the injection into the ureter or renal pelvis through the ureteral catheter of certain silver preparations, of which collargol in 10 per cent. solution stands foremost. Other useful preparations are silver iodide, in 5 per cent. emulsion, cargentos, and argyrol. In this manner graphic representations of the extent and character of dilatation of the ureter and renal pelvis may readily be obtained, clarifying the diagnosis of hydroureter, hydronephrosis, pyonephrosis, etc., incident to obstruction due to bladder retention and ascending infection, extra-ureteral pressure, stricture, and calculus. The characteristic bizarre figures of the distorted pelvis occasioned by the irregular growth of kidney tumors is easily recognizable. Congenital malformations, as fused or horseshoe, solitary, supernumerary, and pelvic kidneys, anomalous ureters and movable kidneys, with twisted or angulated ureters, can best and often only be demonstrated clinically by skiagraphic injections.

SYPHILIS. No disease to which man falls heir has been so thoroughly, effectively, and profitably studied in the past decade as syphilis. The years 1905, 1906, and 1909, representing respectively the discovery of the cause, the most important aid in diagnosis, and a valuable addition to the treatment of the disease, form a triad never to be forgotten in the annals of syphilology. Today the inflexible rule never to start the treatment of syphilis until the diagnosis is surely established, remains just as imperative as in the past; but we are invariably in a position to formulate that diagnosis much earlier, and there is little excuse to await the secondaries for diagnostic purposes. Nor are we obliged to depend upon the Wassermann reaction in the primary stage, since this may be negative even in the absence of treatment until the fifth week. Although the fixation of the complement test is undoubtedly the most useful and reliable means for determining the presence of syphilis, we have, especially in the primary stage, when serum diagnosis may avail naught, other procedures permitting of the correct judgment of the lesion in the first day or two, at the time when intensive modern treatment apparently may effect a speedy cure.

The Dark Field Illuminator. By virtue of the construction of this apparatus, consisting of a microscope fitted with a special

substage reflector, whereby the rays from a powerful source of light are brought to a focal point 1 mm. above the ground illuminator, any solid body, as the *Treponema pallidum*, intercepting these rays at their focal point, will appear luminous; all else is invisible, and forms a dark or black ground. The principle is precisely that observed when a beam of light penetrates a hole and illuminates the dust in a dark room. With this device the discovery of the *Treponema pallidum* in the early chancre, often long before the serum reaction becomes positive, is a comparatively simple act, and seldom fails to disclose the causative organism in the primary lesion of syphilis. Success depends upon the proper preparation of the specimen, and consists largely in the preliminary cleansing of the sore with warm water, followed by firm pressure to obtain a free exudation of lymph or serum containing as few red blood cells as possible. So constant are the findings by this method, and so important is it to establish the diagnosis, early in view of the most successful treatment, that I consider the dark ground illuminator an indispensable addition to the diagnostic armamentarium of each syphilographer for the proper and best handling of his cases.

The Stained Smear. A less reliable method for the demonstration of the *Treponema pallidum* is the stained smear. Many good stains have been suggested for this purpose, but there is one to which I especially desire to direct your attention. It is that by the eosin-azur method, previously described in this paper in connection with the diagnosis of gonorrheal urethritis. The stain possesses differential properties, the treponemas appearing faintly purplish. I know of no stain which so ably fulfils the requirements both for gonococcus and treponema. In doubtful primary sores, if the dark field illuminator be not at hand an attempt, repeated if necessary, should always be made by this method to demonstrate the treponema. Caution must be exercised in the preparation of the smear and the differentiation of the *Treponema pallidum* from the microdentium, pertenuis, and *Spirochæta refringens* is imperative.

Levaditi's Tissue Stain. By recourse either to smear or tissue-stained preparations the *Treponema pallidum* has been demonstrated in every lesion of syphilis. The best method for histopathologic demonstration is Levaditi's modification of the Ramón y Cajal silver-nitrate stain. This procedure has been largely superseded by the serum test of Wassermann, hence its technique will not be described.

Noguchi's Luetin Test. Noguchi is the first investigator to have succeeded, unquestionably, in growing in pure culture the *Treponema pallidum*. Thus he was enabled to accomplish what many others had attempted—namely, an allergic response in syphilitics analogous to the von Pirquet specific cutaneous tuberculin test

as applied to tuberculosis. His luetin is a fluid preparation made by grinding in a mortar the ascitic fluid agar and the ascitic fluid growths, cultivated anaërobically in the presence of pieces of placental tissue. This is sterilized, as is customarily the case, in the preparation of bacterins and standardized by the dark field microscope.

After sterilization of the skin of both arms at the sites selected for the inoculations, one arm is injected intradermically, using a fine needle, with 0.05 c.c. of luetin in two places; the opposite arm is injected with a control emulsion. Normal or negative reactions commence to recede always within seventy-two hours. Positive reactions may assume one of three forms, the papular, the pustular, or the latent. They make their appearance in twenty-four to forty-eight hours up to the fourth or fifth day, and in the latent form may light up even after the tenth day. In an analysis of 400 cases, Noguchi has found that the luetin test is not as reliable as the complement-fixation test in the primary, secondary, and parasyphilitic stages; he found it most servicable in the tertiary and hereditary manifestations of the disease, being positive in 100 per cent. of manifest tertiary affection and 96 per cent. of hereditary syphilis. The test should certainly prove of great value, particularly when improvements in the preparation and potency of the luetin are possible, to those practitioners not being in a position or not caring to employ the Wassermann reaction.

The Butyric Acid Test. This method, suggested by Noguchi for the detection of the active lipotropic syphilitic antibodies in the cerebrospinal fluid and blood serum, depends upon the precipitation of globulin on the addition of butyric acid. The application of the test varies somewhat whether the spinal fluid or blood serum is employed. Noguchi himself seems not particularly impressed with the blood application of the test, but claims in certain neurologic syphilitic manifestations that it supersedes in reliability and value the Wassermann reaction. This assertion has not been accorded universal confirmation where the most approved technique for the complement-fixation test has been employed. Nevertheless the reaction occurs quite regularly in the cerebrospinal fluids of patients with syphilitic and parasyphilitic affections, and runs a parallelism with the cytodiagnosis of parasyphilitic disease. In addition to syphilis the reaction occurs in many of the other diseases involving the central nervous system, as influenza, pneumonia, tuberculosis, cerebrospinal meningitis, anterior poliomyelitis, etc., but these conditions are usually readily differentiated or excluded. The test is unquestionably of great value, and irrespective of its relative comparison with the Wassermann reaction, because of its simplicity can be carried out in any laboratory.

The Wassermann Reaction. Time and desire at present exclude a detailed consideration of the technique of the complement-

fixation test for syphilis. The most brilliant modification of the Wassermann reaction is that by Noguchi. Theoretically, employing the most approved technique, Noguchi's method would have more to recommend it if it were more simple in its performance than the Wassermann. Noguchi's contention that his method is more delicate in the detection of the syphilitic antibody than the Wassermann technique, the inaccuracy of which depends upon an unknown amount of natural hemolytic amboceptor in the patient's serum against sheep's red blood corpuscles, has not been confirmed in the experience of those employing the best Wassermann technique, wherein a standardized complement unit, a properly titered hemolytic amboceptor, together with careful standardization of red blood corpuscles and antigen are used.

That the complement-fixation test of Wassermann is the most valuable and reliable diagnostic aid for syphilis in general is no longer disputable. Positive reactions, with the following exceptions, which can almost invariably be excluded in other ways, mean syphilis. The exceptions are in yaws, relapsing fever, trypanosomiasis, tubercular leprosy, certain drug narcoses, as from morphin, scopolamin, veronal, and ether, and in sera obtained just before or after death. It is plausible to think that when in the performance of the reaction, specific antigen of a pure culture of *Spirochætæ pallida* instead of the customary lipotropic substances can be employed the exceptions may be rendered fewer.²

A negative reaction, on the other hand, does not mean necessarily that syphilitic infection is absent. Treatment, whether by mercury or Ehrlich's arsenical preparations, may prohibit the occurrence of a positive reaction for a few days to many months. This of course depends upon the virulence of the infection on one hand and upon the intensity of the treatment on the other. I have repeatedly observed after a moderate mercurial administration a negative reaction for several days, which after two or three weeks became positive. On the contrary in the latent stage of the disease, when the serum may exhibit a negative Wassermann reaction, a provocative positive reaction may be elicited by multiple injections of mercury or by the administration of 0.02 to 0.05 gram of salvarsan or neosalvarsan. However in the absence of any treatment following the appearance of chancre I have never seen a case in which a negative reaction persisted for a longer period than four weeks. In the event of insufficient treatment I have seen many reactions continuously negative for six to nine months after the cessation of treatment once more become positive. In view of this, and the fact that approximately one-third of all patients who have passed through the classic mercury and

² Since this article was written and read, investigations along this line by Dr. John A. Kolmer have shown, however, that such is not the case.

iodine form of treatment, even in the absence of symptoms, still give the complement-fixation test, evidencing their proclivity to parasyphilitic lesions, as paresis, locomotor ataxia, etc., we have come to regard the Wassermann reaction employing the standardized single complement-unit as originally suggested by Laird, not the multiple complement-unit system as more important for the control of treatment than for the diagnosis of the disease. Thus as a tentative plan no patient should be discharged cured until he presents for a period of at least two years after discontinuance of treatment a continuously negative Wassermann taken at three-month intervals. Even at the expiration of that time the safest procedure is to repeat the test yearly indefinitely.

I would state that the Wassermann reaction, with proper technique and precautions, has been found as indispensable in syphilology as it is well-nigh infallible.

Salvarsan and Neosalvarsan. The indication for these remedies is popular knowledge. The technique of their preparation for and mode of administration is indifferently and carelessly observed, and I have known fatalities to occur not on account of the drugs themselves but because of the heedlessness or incompetence of the physician. Therefore in the belief that Ehrlich is more familiar with the chemical and potential harmful properties of these synthetic preparations than we are, I think it behooves us to follow strictly his advices in the administration of the drug. Thus he advises in the case of neosalvarsan that the drug should be dissolved in a solution at 68° to 72°, and administered to the patient at that temperature, that it should not be shaken unduly and should be given immediately, because of its unstable characteristic. Although "914" is acknowledged to be not nearly so toxic as "606," two deaths even from neosalvarsan have been reported from Europe.

It is too early to pass judgment finally upon the relative merits of salvarsan and neosalvarsan, but from an experience of several hundred injections I feel convinced that the latter is not so immediately effective as the former preparation at least in the secondary period of syphilis. In practically all stages of the disease, excepting the parasyphilitic manifestations after degeneration of nervous tissue has supervened, we know that these arsenic preparations suffice to produce symptomatic cure, either in single or multiple dosage; respecting their ultimate or permanent curative effect, we know absolutely nothing. A few years must elapse before conclusions can be drawn. At present the treatment of syphilis is truly empiric, although with the promise that we possess in Ehrlich's preparations remedies of paramount importance, capable of shortening very materially the required period of treatment.

Approximately 10 to 20 per cent. of patients studied to date have apparently been cured by single or multiple injections of

salvarsan and neosalvarsan alone, judged by the non-appearance of secondaries and a continuously negative Wassermann for a period of two years. Almost all these have been patients who received the drug during the first week of the chancre. Experience has also shown that with the exception of the first few days of the disease multiple doses, unless contraindications arise, should be administered. Moreover, both from the Wassermann reaction control as well as from the clinical symptomatology, it is obvious that the treatment must be intensive from the start, and that to be most effective the arsenic should precede the mercury. Consequently we have adopted the tentative procedure in all stages of the disease, with the exception of the earliest primary, to administer salvarsan or neosalvarsan, always intravenously, in multiple doses, usually three, at intervals of a week or two unless contraindications exist. Coincidentally the patient is placed on a vigorous campaign of mercury—or if in the tertiary stage, mixed treatment—for six months or a year. On suspension of the mercurial or mixed treatment he is again given one or more injections of salvarsan or neosalvarsan. Thereafter the renewal of treatment or the pronouncement of cure is governed by periodical determinations of the Wassermann reaction.

AN ORTHODIAGRAPHIC STUDY OF A CASE OF BRONCHIAL ASTHMA.

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FLUOROSCOPIC examinations of patients with bronchial asthma have been described by Krause,¹ Dally,² Jamin,³ Levy-Dorn,⁴ Schlesinger,⁵ and others. These have shown a diminished density of the pulmonary tissue, a horizontal position of the ribs, widening of the intercostal spaces, a low, flattened diaphragm, and a heart low and in the median line. The orthodiagraph enables us to

¹ Atlas und Grundriss der Röntgendiagnostik, edited by Franz M. Groedel, München, 1909, pp. 70 to 71.

² On the Use of the Röntgen Rays in the Diagnosis of Pulmonary Diseases, *Lancet*, June, 1903, xxvii, 1800 to 1806.

³ Atlas und Grundriss der Röntgendiagnostik, edited by Franz M. Groedel, München, 1909, pp. 56 to 57.

⁴ Ein Asthmatischer Anfall im Röntgenbilde, *Berlin. klin. Woch.*, 1896, xxxiii, 1046 to 1048.

⁵ Zur Lehre vom Asthma Bronchiale, *Wien. klin. Woch.*, 1898, xi, 265 to 366.

record these changes accurately from day to day. The following case was studied by this method for a period of eight weeks, and is of particular interest in that it shows the slow return to normal after complete cessation of a prolonged attack of asthma.

Mrs. S., aged twenty-seven years, entered the University Hospital on January 29, 1912, suffering from bronchial asthma. Her attacks of asthma began at the age of nine years. After a brief period of relief about the time of puberty these attacks reappeared at the age of fifteen. She was married at seventeen and remained practically well until twenty years of age. During this interim three children were born, but after the birth of the last child the attacks recurred. Since 1907 the attacks have become more severe and have frequently lasted for weeks at a time, leaving the patient in a weakened condition. All the customary remedies have been tried, but none have proved reliable in preventing or aborting her attacks.

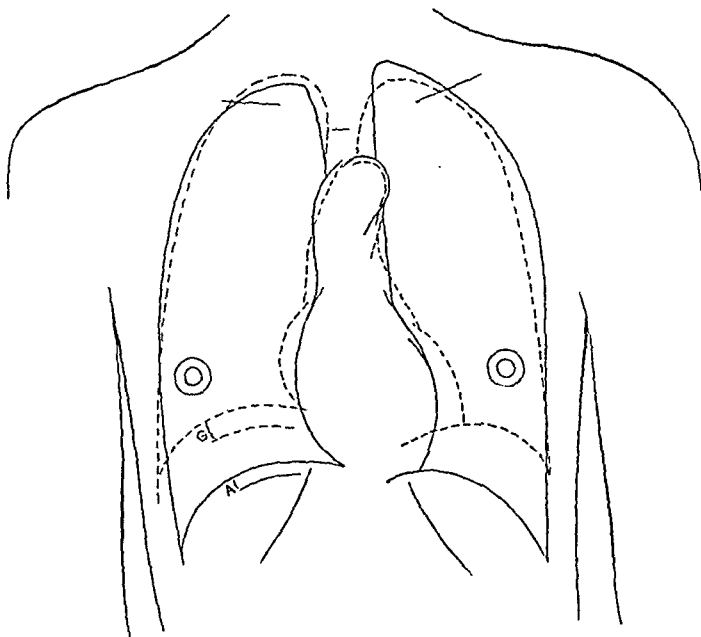
The patient entered the hospital toward the end of a prolonged attack of asthma, which had confined her to bed for four months. She had been receiving, hypodermically, as much as a grain and a half of morphin a day, for this seemed to be the only method of relieving her severe dyspnea.

Examination showed moderate emaciation. She was markedly dyspneic and the accessory respiratory muscles were used constantly. The anteroposterior diameter of the thorax was increased and the borders of pulmonary resonance unusually low. Costo-sternal joints moved freely. No rales were heard over the thorax on the day following her admission and none thereafter during her stay in the hospital. Almost immediately after coming into the hospital the severe symptoms abated without the use of any medicine. The morphin was withdrawn and the patient's general condition gradually improved. She was discharged March 23, 1912, in good condition, save for slight dyspnea on exertion.

One month later she returned to the hospital, shortly after the onset of a fresh attack of asthma. On this occasion numerous musical rales were heard over all parts of the chest; this attack also subsided while in the hospital. At no time did the blood show an eosinophilia or the sputum Curschmann spirals. Aside from these, however, the patient seemed to have had a typical bronchial asthma.

An orthodiagraphic examination made the day following the first admission showed an extreme degree of pulmonary distention, with a low and flat diaphragm and the heart in the vertical position (see diagram). It is well known that pulmonary distention accompanies bronchial asthma, but its exact extent and its duration after the attack has never, to our knowledge, been accurately determined by means of the orthodiagraph. The impression seems to prevail that the acute pulmonary distention of asthma

usually disappears promptly after the attack, although Jamin states that a less marked distention may possibly remain for some



Continuous line shows position of diaphragm, heart and lung borders at entrance. A indicates diaphragm excursion at height of distention. Dotted line shows position of same organs at discharge. Note diaphragm excursion (G) at this time.

indefinite time. Our patient continued to show a diminishing lung volume over a period of seven weeks. The gradual changes are shown in the following chart.

TABLE I.

Date.	Area ⁶ of right lung.	Area of left lung.	Total lung area.
January 29, 1912	185.5 sq. cm.	173 sq. cm.	358.5 sq. cm.
February 8, 1912	167.0 sq. cm.	163 sq. cm.	330.0 sq. cm.
February 12, 1912	158.0 sq. cm.	165 sq. cm.	323.0 sq. cm.
February 16, 1912	152.0 sq. cm.	158 sq. cm.	310.0 sq. cm.
February 27, 1912	148.0 sq. cm.	156 sq. cm.	304.0 sq. cm.
March 5, 1912	143.0 sq. cm.	145 sq. cm.	288.0 sq. cm.
March 9, 1912	142.0 sq. cm.	152 sq. cm.	294.0 sq. cm.
March 16, 1912	146.0 sq. cm.	146 sq. cm.	292.0 sq. cm.
March 21, 1912	137.0 sq. cm.	132 sq. cm.	269.0 sq. cm.

On the second admission the following areas were found as the condition improved.

TABLE II.

Date.	Area of right lung.	Area of left lung.	Total lung area.
April 22, 1912	174.0 sq. cm.	173.5 sq. cm.	347.5 sq. cm.
April 26, 1912	178.6 sq. cm.	183.5 sq. cm.	362.1 sq. cm.
May 6, 1912	157.2 sq. cm.	139.0 sq. cm.	296.2 sq. cm.
May 8, 1912 ⁷	147.5 sq. cm.	146.0 sq. cm.	293.5 sq. cm.

⁶ These areas were measured by the planimeter on orthodiagraphs taken in the usual antero-posterior directions.

⁷ At this date the patient left the hospital, although her lung area had not reached the lowest point seen on the previous admission.

This gradual subsidence of the pulmonary distention derives particular interest from its possible relation to permanent pulmonary distention in chronic emphysema. Acute distention of the lungs, such as occurs during exercise, is known to pass off almost immediately (Bohr⁸) or to last at most only a day or two (Durig⁹). The effect of repeated and prolonged distention, such as may occur in severe bronchial asthma or in chronic bronchitis, is less well understood. It is commonly held by clinicians that these may lead to permanent pulmonary overdistention, even after the exciting causes have disappeared; yet the proof of this by objective methods has not been furnished and other theories have been advocated to account for chronic pulmonary overdistention. So far as our patient is concerned the obstructions in the bronchi, as judged by an absence of rales, cleared up shortly after she first entered the hospital, and it seems to us that the slow return to a normal lung volume can best be explained on the assumption of a partial loss of pulmonary elasticity with slow recovery. Our observations therefore favor the view that a severe and continued overdistention of the lungs, due to obstruction in the bronchioles, may exert a prolonged effect on the pulmonary volume even after the cause has disappeared; and it seems probable that if attacks of asthma continue, or if the lungs are damaged by disease or by age, a permanent distention might result from this cause.

While it is generally agreed that the diaphragm is low during the attacks of asthma, there have been differences of opinion regarding its movements. Levy-Dorn first described a unilateral immobility of the diaphragm during an attack of asthma. While viewing the patient a fit of coughing terminated the attack and the diaphragm then began to move. He ascribed this immobility to the pressure of the greatly inflated lung and not to a spasm of the diaphragm. Dally has observed the same phenomena. Jamin observed that the motion of the diaphragm was greatly diminished in comparison with the strong respiratory movements of the thorax. He noted that the diaphragm moved downward slowly on inspiration and returned much more slowly to its position during expiration. Krause observed nine cases, in four of which he noted an immobility of one-half of the diaphragm, three times on the right and once on the left side. The other half of the diaphragm made short, quick, jerky movements with an excursion much less than the normal. He believed that there was a unilateral spasm of this muscle. As the condition returned to normal the spasm gradually lessened and the movement of the two halves of the diaphragm became equal and uniform. In five other cases he noted jerky

⁸ Die Funktionellen Aenderungen in der Mittellage und Vitalkapazitaet der Lungen, Arch. f. klin. Med., 1907, lxxv, 385.

⁹ Ueber die Groesse der Residualluft, Centralb. f. Phy., 1903, xvii, 258 to 267.

movements of the diaphragm, with small excursion of both halves. Both sides were distinctly mobile. On the first examination our patient showed slight movements of the diaphragm on both sides, but the extent of the movements (as seen in the diagram) was much less than normal. As the pulmonary distention disappeared the diaphragmatic movements gradually increased and reached their maximum at the end of her stay in the hospital. At this time the diaphragm stand was 3 cm. higher than its position at the beginning of the attack, and the respiratory excursion had increased from 0.5 cm. to 1.5 cm. On the second admission, during an attack, there was no spasm of the diaphragm observed, but the right side moved slightly upward during inspiration and downward during expiration. We are inclined to explain these paradoxical movements as due to a relatively motionless diaphragm, which was carried up and down by the excessive thoracic movements.

As described by Levy-Dorn the heart in asthma is low with the apex in the sixth interspace near the sternum, the right border reaching considerably beyond the sternum. Moritz showed a diminution in the size of the heart in one case, and Goetzl and Kienboch¹⁰ observed the same during an attack in two cases. Dietlen¹¹ reports six cases in which the heart shadow was determined during an attack in both inspiration and expiration. He observed that the heart silhouette was smaller during expiration than during inspiration, which is the reverse of that usually found in normal man, and he explained this as due to the increase of intrathoracic pressure during expiration, which obstructed the venous inflow and possibly compressed the heart. The heart of our patient on entrance was in the vertical position (Fig. 1), and it showed a surface area of 64 sq. cm. As the pulmonary distention lessened the heart became less vertical, and although its shape varied somewhat from time to time the surface area remained almost constant.

TABLE III.

Date.	M. R.	M. L.	Total width.	Area of heart.
January 29, 1912	2.5 cm.	5.5 cm.	8.0 cm.	64 sq. cm.
February 8, 1912	3.0 cm.	5.4 cm.	8.4 cm.	60 sq. cm.
February 12, 1912	3.9 cm.	5.5 cm.	9.4 cm.	66 sq. cm.
February 16, 1912	2.9 cm.	7.6 cm.	10.5 cm.	67 sq. cm.
February 27, 1912	3.9 cm.	5.7 cm.	9.6 cm.	67 sq. cm.
March 5, 1912	4.1 cm.	5.7 cm.	9.8 cm.	61 sq. cm.
March 9, 1912	4.0 cm.	5.4 cm.	9.4 cm.	63 sq. cm.
March 16, 1912	4.3 cm.	5.2 cm.	9.5 cm.	61 sq. cm.
March 21, 1912	4.1 cm.	5.7 cm.	9.8 cm.	62 sq. cm.

¹⁰ Asthma bronchiale und Verkleinerung des Herzens, Wien, klin. Woch., 1908, xxi, 1261 to 1265.

¹¹ Orthodiagraphische Untersuchungen über pathologische Herzformen und das Verhalten des Herzens bei Emphysema und Asthma, Münch. med. Woch., 1908, lv, 1770 to 1773.

CONCLUSIONS. In a patient with severe and repeated attacks of asthma the pulmonary distention continued for several weeks after a cessation of a prolonged attack. This distention caused the heart to assume a vertical position, but did not influence its surface area. During the attack of asthma the diaphragm moved but slightly, and movements in reverse of the normal were observed. In explaining such reversed movements, however, one must take into account the excessive thoracic movements which act on the diaphragmatic attachments. The movements of these attachments may more than neutralize the movements due to the diaphragmatic contractions, so that the crests of the diaphragm may seem to execute reversed movements.

A CONTRIBUTION TO THE STUDY OF HEREDITARY DEGENERATION (PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY IN COMBINATION WITH DEGENERATION IN THE CENTRAL NERVOUS SYSTEM).

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WHEN only certain parts of the nervous system are congenitally defective they are likely to be those having close functional relations to each other, and in consequence there develop in such cases certain functional disturbances which enable the nature and location of the anatomic lesion to be diagnosticated with accuracy. It is well known also that these defects may not be apparent until the individual has attained a certain age, when, seemingly from the mere stress of living, the defective parts undergo retrogressive changes, and symptoms of disability appear, the nature of which depends upon the functions of the part affected. In these cases of so-called abiotrophy a strong reason for believing that the anatomic change and the resulting clinical phenomena are congenital in origin is their tendency to become a characteristic of certain families.

The literature of these family degenerative conditions is quite extensive, but for the most part the published studies on the subject may be divided into those which deal with the localization and character of the histopathologic changes in the nervous system or other tissues involved and those concerned with attempts to classify them into types according to the symptoms presented or the parts affected, which are then considered as separate and

distinct diseases. A study of the literature leads to the conclusion that there are in all these cases histopathologic changes of a degenerative character in the various tissues, and that the clinical types depend largely, if not solely, on the location of the lesion. From this it follows that if there was present in the parental organism a toxic substance or disease capable of causing degenerative changes in the nervous system or elsewhere, and this toxic substance or disease could be transmitted to offspring, those offspring might show similar degenerative changes. Under such circumstances we would be dealing not with an hereditary degeneration but with a degeneration due to disease or toxemia possibly preventable or treatable. The question arises whether we have any way of differentiating a truly hereditary characteristic from an acquired degenerative condition caused by a neurotoxin transmitted from parent to child.

These dystrophies, when they affect the nervous system, give rise to various fairly definite symptom-complexes, such as Friedreich's ataxia, family spastic paraplegia, etc. The muscular dystrophies are also divided into various types: the pseudohypertrophic form of Duchenne; the juvenile form described by Erb; Leyden's form; the facioscapulohumeral type (Landouzy-Dejerine); Zimmerlin type, beginning in the thorax muscles and affecting the upper extremities before the lower; a type described by Jendrassik as congenital, that is, the manifestations begin at birth; and the Werdnig-Hoffman type, beginning in infancy and affecting several members of the same family, but so frequently these types are combined with each other or present anomalous characteristics that we have the authority of Erb¹ that their differentiation is a matter of great difficulty. They are usually familial, and are regarded as quite distinct from the spinal type of progressive muscular atrophy; and from the neural, or Charcot-Marie-Tooth type, variations of which are described by Gombault, Dejerine-Scottas, Eichorst, Brossard, and others. It is certain, however, that progressive spinal muscular atrophy may be hereditary, as in the case reported by A. Strümpell² and in a similar case reported by Bernhardt.³ If such is the fact we have an instance of a condition usually regarded as due to some unknown, acquired cause becoming hereditary. There are two possible explanations: one is that an acquired degeneration has become hereditary, which is opposed to Weismann's theory of heredity; or that the cause of the degeneration in the parent was transmitted to the offspring and became in turn the cause of the degeneration there. The observations of William G. Spiller⁴ that syphilis might be a cause

¹ Deutsch. med. Woch., 1910, S. 1865.

² Deutsch. Zeitschr. f. Nervenheilk., 1893, Band iii, S. 471.

³ Virchow's Archiv, Band cxv, Heft 2, S. 197.

⁴ Jour. Nerv. and Ment. Dis., 1912, p. 584.

of the so-called primary lateral sclerosis and of progressive spinal muscular atrophy, and the case recorded by S. Leopold⁵ of progressive spinal muscular atrophy, in which necropsy showed some evidence of syphilis, suggests at least one such cause that can be acquired and can also be transmitted to the offspring.

As bearing on this question, I wish to record a case observed by me in which a parent and probably also a grandparent had the spinal type of progressive muscular atrophy, while the patient presented the classical picture of the pseudohypertrophic form of muscular dystrophy. The occurrence of such a case indicates a close relationship between these two conditions.

John C., aged three years, was admitted to the Hospital of the University of Michigan November 20, 1909. His mother was well. His father could not be examined, but, according to the description furnished, was suffering from a disability which began with wasting of the small muscles of both hands, producing a clawhand, and this wasting had extended up both arms to the shoulders. The affection was painless and not accompanied by any change in the sensibility of the hands, and there was no involvement of the lower extremities. It may be inferred that he was suffering from the progressive muscular atrophy of the spinal type. Chronic anterior poliomyelitis may be ruled out by the statement that the atrophy was quite pronounced before any marked weakness was noticed. There was also a statement that the patient's grandfather on the father's side had an affection similar to the father's, but an accurate description of his condition was unobtainable. The mother of the patient had had one miscarriage before he was born, and the patient had a younger brother apparently well.

The patient was born at full term, with instruments, and was seemingly normal and uninjured. He learned to talk at the age of ten months and to walk at one year. He had measles in the summer before his admission to the hospital, and a light attack of pneumonia at the same time. His present trouble apparently began when he was about the age of two years, when some difficulty in walking was noticed, and this became progressively worse until his admission to the hospital. An examination at that time showed a child of about normal size for his age, hair light and fine, a well-nourished appearance, intelligent expression, and a well-shaped head. He understood and obeyed commands, answered questions readily, and appeared to have a normal mentality. The pupils were equal, reacted to light and in accommodation, and there were no extraocular palsies. The ocular fundi appeared normal. There was no paralysis of the face or tongue. The arms, forearms, and shoulders were rather thin, but all movements were normal, and there was no fibrillary tremor. There was no atrophy of the small

muscles of the hands. When standing there was a marked lumbar lordosis and protrusion of the abdomen; this was present also when sitting or lying on his side; it disappeared when lying on his back. There was no lateral curvature of the spine. The thighs appeared to be about the normal size, but the calves of both legs were distinctly larger than normal, and felt very firm. There was no paralysis or deformity of the legs or feet and he could walk without support, but has a waddling, typically dystrophic gait. In arising from a prone position he turned over and rose on his hands and knees. He then attempted to rise to a standing position by pushing with his arms, but was apparently too weak to so do without assistance. The biceps-jerks were present on both sides, but the knee-jerks and Achilles-jerks were not obtained. No sensory loss could be detected anywhere. The skin reflexes were all present. Plantar irritation caused flexion of the toes.

While the age of the patient suggests the Werdnig-Hoffman type of muscular dystrophy, a pseudohypertrophy such as was present here rules out that diagnosis according to Hoffman.⁶ We have then an instance of progressive spinal muscular atrophy in the father and grandfather and pseudohypertrophic muscular dystrophy in the child. I have not been able to find a similar case of heredity in the literature, but K. Mendel⁷ reported a case in which the symptoms of progressive spinal muscular atrophy were combined with those of a pseudohypertrophic muscular dystrophy in a boy, aged sixteen years. The condition was not hereditary.

Eulenberg and Cohn,⁸ under the title of "family dystrophic heredodegeneration," reported four members of the same family, aged from eight to sixteen years, affected with a progressive muscular atrophy beginning in the face and upper extremities and accompanied by pseudohypertrophy of the calves and lost knee-jerks, but they regarded these cases as a peculiar type of muscular dystrophy rather than as a combination of types.

While the dystrophies are usually hereditary, and thereby differ from the progressive spinal muscular atrophies which are not, usually, there are many cases of muscular dystrophy in which no hereditary influence can be detected. I have seen a boy, aged twelve years, suffering from a typical muscular dystrophy of the pseudohypertrophic type, but the most careful inquiries failed to show any trace of hereditary degeneration. The parents were healthy and not blood relations. They had two other children, one older and one younger than the patient, who were normal. All of the grandparents and the aunts and uncles of the patient were living, and showed no apparent abnormality. The patient

⁶ Deut. Zeitschr. f. Nervenheilk., 1893, S. 427; *ibid.*, 1897, S. 292; *ibid.*, 1898, S. 418.

⁷ Neurolog. Centralbl., 1901, S. 601.

⁸ *Ibid.*, 1911, S. 963.

presented typical signs and symptoms of the disease, which it would be unnecessary to record in detail.

It is not uncommon to find atypical cases of muscular dystrophy or combinations of two or more types in the same patient, as Erb has pointed out. It is, however, much less common to find the combination of a muscular dystrophy with the spinal heredo-degenerations. Such cases do occur, however, and are of considerable clinical importance, primarily because of the liability to errors in diagnosis.

The following case is an instance of the combination of Friedreich's ataxia with a pseudohypertrophic muscular dystrophy in the same patient:

Carl K., aged ten years, was admitted to the Hospital of the University of Michigan July 24, 1912. On his admission the following history was obtained from his parents:

His father and mother were living and well, and the patient had two sisters, one five years old and one seven, both in good health. There were no nervous disorders on the father's side of the family but the mother said that she had two brothers; the older one was well, but the younger one had an affection similar to the patient's, coming on at the age of ten and causing his death at the age of eighteen years. Her father and his brothers were free of any nervous disorder, but her mother's brother had a similar complaint, beginning at ten and fatal at eighteen years.

The patient was a first child, and was delivered with instruments, but apparently not hurt. He was bottle-fed, and had diarrhea in his first year. He walked and talked at about the usual age, and appeared to be a normal child. Measles and whooping cough were the only infectious diseases he had, and there was no history of injury. He had never had any convulsions.

At an early age, about four years, it was noticed that he had some difficulty in walking—a waddling gait—and this difficulty slowly increased; but about one year before his admission to the hospital his gait became much worse, and it was noticed that he walked on his toes. About June 1, 1912, he became unable to walk at all. He had severe headaches for about a year, usually coming two or three times a week, and his father stated that his school work was poor for this year; he seemed to have difficulty in learning, and also was forgetful. He had no other symptoms.

On examination, July 26, 1912, it was noted that he seemed to be a well-nourished, intelligent boy, with few stigmas of deviation and no stigmas of hereditary syphilis.

The pupils were equal, and reacted to light and in accommodation. There was a distinct nystagmus on lateral deviation of the eyeballs. There was no paralysis or atrophy of the face or tongue. There was no disturbance in speech or deglutition. The grip of both hands was weak, especially the left. He could raise both

arms above his head, but his power to resist passive movement of the elbows and shoulders was less than normal. There was no atrophy or deformity of the hands, arms, or shoulders, no fibrillary tremor and no ataxia in the finger to nose test, with the eyes open or closed. The biceps-jerks and triceps-jerks were not obtained on either side. The patient sat in his wheel chair leaning forward on his elbows. He could not walk and could stand only if all his weight was supported from his shoulders. He stood on his toes. The thighs and buttocks were normally developed for his age, but the calves of both legs were abnormally large and felt firm on pres-



FIG. 1.—Pseudohypertrophic muscular dystrophy and Friedreich's ataxia, showing the 'Friedreich foot.' The foot is shortened, and there is permanent hyperextension of the proximal phalanx and flexion of the terminal phalanx of the great toe. Note also the pseudohypertrophy of the calf muscles.

sure. There was a distinct talipes equinus in both feet, with hyperextension of the first phalangeal joint of the great toes and flexion of the terminal joint (Fig. 1). There was no atrophy of the small muscles of the feet. All normal movements of the legs and feet were possible but weak. The knee-jerks were present on both sides, but were diminished. The Achilles-jerks were present on both sides. Plantar irritation caused extension of the great toe on each side. The cremasteric and abdominal reflexes were present on both sides. Tactile sensation was normal on the face, body, and extremities, and the localization of sensation was normal on

the legs and feet. There was no analgesia or thermesthesia, and no loss of the sense of motion or position in the fingers or toes. A general physical examination was negative. The urine examination showed a specific gravity of 1020; no albumin; no glucose; no bile; urea, normal amount; sediment was normal. An examination in the ophthalmologic clinic, by Dr. Walter Parker, showed: nystagmus on lateral deviation of the eyeball; pupils equal; reflexes normal; no gross lesion.

July 29. Began taking x-ray treatments to the spine three times a week. A "soft tube" was used and the distance about 12 inches. Ten minutes exposure was given the entire spine.

July 31. Blood count showed: red blood cells, 4,500,000; leukocytes, 10,000; hemoglobin, 85 per cent.

He was re-examined in August and September, with practically the same findings. The headaches entirely disappeared after the first week of x-ray treatments, and he was able to stand by grasping a small topped table and resting his chest against it. In standing this way his back was bent forward and his legs widely separated; if the buttocks were supported he showed a marked lumbar lordosis. Irritation of the soles of the feet produced extension of the toes on each side and also a movement of withdrawal of the entire leg ("reaction of defence," Babinski). A general physical examination showed nothing pathologic in the viscera, no glandular enlargement, and a normal development of the external genitalia. A Wassermann reaction on the blood was negative, and examination of the cerebrospinal fluid showed no abnormal chemical or cellular constituents.

Cases of Friedreich's ataxia and muscular dystrophy have been reported by Jendrassik,⁹ with an anatomic study by Kollaritis.¹⁰ Cases are also reported by Baumlin¹¹ and Bing.¹² A similar case but without any family history of either disease is reported by Jastrowitz.¹³ Cases of muscular dystrophy, such as the one reported by O. Crouzon,¹⁴ in which there was present a positive Babinski sign, and that of H. Schlesinger,¹⁵ in which the patient developed a pes equino valgus in both feet early in the disease, are cases somewhat resembling these. Greenfield¹⁶ reported a case of Friedreich's disease combined with the peroneal type of progressive muscular atrophy. Cases of spastic spinal paralysis, nystagmus, and tremor are reported Jendrassik,¹⁷ who refers to similar cases

⁹ Deutsch. Zeitschr. f. Nervenheilk., 1902, S. 444.

¹⁰ Deutsch. Archiv f. klin. Med., 1901, Band lxx, S. 157.

¹¹ Deutsch. Zeitschr. f. Nervenheilk., 1901, S. 265.

¹² Deutsch. Archiv. f. klin. Med., 1905, S. 199.

¹³ Neurolog. Centralbl., 1911, S. 426.

¹⁴ Revue Neurologique, 1912, p. 109.

¹⁵ Neurolog. Centralbl., 1901, S. 143.

¹⁶ Proc. Royal Soc. Med., London, v, No. 3, Neurol. Sec., p. 75.

¹⁷ Deutsch. Archiv. f. klin. Med., 1897, Band lviii, S. 137.

reported by Maas, Seeligmüller, and Hoffman. These cases probably represent still another combination of heredodegenerative conditions.

A case of pseudohypertrophic muscular dystrophy combined with optic neuritis is not mentioned by Jendrassik¹⁸ in his collection of transitional and combination types of heredodegenerations. Such a case was admitted to my service at the Hospital of the University of Michigan May 27, 1912:

Floyd B., aged eight years, complained chiefly of difficulty in walking. No history of the case was obtainable except from the patient himself, who said that his mother was dead and that his father had deserted the family. He said that he had three brothers, and they all had trouble similar to his. He did not remember that he ever had any serious illness, but said that he never went to school and that he could not read or write. An examination on his admission to the hospital showed a pleasant, well-mannered child, who obeyed all simple commands, dressed and undressed himself, untied knots normally, and was about the average size for a child of nine years. His head was of normal shape, his ears rather prominent, and Darwin tubercles were present on both ears. The pupils were equal, reacted to light and in accommodation. The extraocular movements were normal. There was no facial palsy. The tongue protruded straight, and there was no tremor or atrophy of the tongue. The masseters and temporals contracted well and equally. He had no difficulty in moving his head. There was no tremor of the hands on extension. There was no disturbance of the gross movements of the arms, and there was no incoördination of the hands in the finger to nose test. The muscular strength in the arms in flexion and extension was equal and good in both arms. There was no atrophy or deformity of the arms or hands and no fibrillary tremors were noticed. The grip was equal and good in both hands. The patient walked with a broad base, but there was no ataxia and no apparent spasticity in the legs. His station was equally as good with his eyes open as with them closed. There was marked weakness in extension of the legs and dorsoflexion of the feet equal on both sides. The muscular strength in flexion of the legs was fair. Both extension and flexion of the thighs were weak, although the patient could flex and extend the thighs if no resistance was offered. On standing erect there was a forward curvature of the lumbar spine and bulging of the abdomen. He appeared to elevate the hips in walking. The musculature of the calves of the legs appeared large and bulging (Fig. 2). No unusual development in the musculature of the thighs was present, and there was apparently no atrophy of the thigh muscles. He felt pinpoint equally well over both sides

¹⁸ Lewandowsky's *Handbuch der Neurologie*, Berlin, 1911, Band ii, S. 397.

of the face. There was no anesthesia of the conjunctivæ. He felt pinpoint and light touch over both sides of the back, both sides of the abdomen, and both sides of the thorax. Pinpoint was felt equally well over both lower extremities all over. There was no disturbance of sensation of any form over the arms. The elbow-jerks and knee-jerks were not obtained. The Achilles-jerks were equal and about normal. The conjunctival reflex was present. The umbilical reflex and the cremasteric reflexes were present. Plantar irritation caused plantar flexion of the toes on both sides. He was well-nourished, and an examination of the heart, lungs, and abdominal viscera showed nothing abnormal. The examination of the blood and urine was negative. The blood pressure was 115 mm. Hg. A Wassermann reaction on the blood was reported negative.

May 31. Patient was examined by Dr. Walter Parker, who found: Tension O. U., normal. Pupillary reflexes active, normal to direct and consensual light and in accommodation.

Ophthalmoscopic examination: O. D., media clear. Disk margins completely blurred, slightly hyperemic, swollen between 1 and 2 diopters. The temporal side of the disk at the area of the muscular bundle apparently was not swollen. There were some irregular grayish-white changes near the nasal border of the disk, with one or two spots of pigment; these changes were like irregular, inconspicuous branched lines. There was a peculiar stippling of the whole fundus quite marked between the macula and the disk. The veins pulsated. O. S., the disk was swollen, particularly on the nasal side, and there was an oblique position of the disk, the obliquity being so great that the disk seemed to face toward the macula, and the temporal side of the disk was nearly obscured. This was undoubtedly due to an oblique position of the

scleral foramen, the optic nerve entering obliquely. The apparent amount of swelling was 3 diopters.

Choroid: There was an area of choroidal change near the nasal border of the disk nearly a disk diameter in size. In this area there was some pigment displacement and a short, crescent-shaped



FIG. 2.—Pseudohypertrophic muscular dystrophy and optic neuritis.

streak, lighter in color at the outer border of the pigmented area, nearly parallel to the disk border. At the nasal border of the disk there was a small, grayish, rounded area about one-half disk diameter in width, over which the retinal vessels could be distinctly seen. The whole choroid was stippled with grayish pigmentation. There were no pigmentary changes in the periphery of the fundus.

Diagnosis: O. D., optic neuritis. O. S., same as O. D., with localized choroiditis. Two months later the condition was unchanged.

The diagnosis of pseudohypertrophic muscular dystrophy can be made in this case with certainty, but most interesting is the presence, in association with this condition, of a bilateral optic neuritis of a peculiar type. That this is an example of hereditary optic neuritis seems most likely, for the reason that all the details of the ophthalmoscopic findings correspond closely to those described by Hormuth¹⁹ as present in such cases. Furthermore, there was a family history of some similar affection and an absence of any symptoms or signs of intracranial disease to cause optic neuritis and no history or sign of any poisoning.

While the most obvious interest in the cases above recorded lies in questions of diagnosis, they are perhaps more valuable for the evidence they furnish as to the etiology of such conditions. In the cases of dystrophy ordinarily seen there is a tendency to the transmission of the same type of defect from parent to offspring usually a fairly definite type, and the defect apparently is transmitted as are other family traits. If all cases were of that kind there would be little objection to the view that "heredity" was a sufficient etiology, even though we would still be in the dark as to the primary causal factor. When we find a case in which one type in a parent is followed by another type of degeneration in the offspring, or when, as in the last two cases, we find degenerative changes variously localized, it seems more probable that something truly external is acting on the organism, attacking the weaker parts. Generally, true heredity acts in a way which is distinctly opposed to degeneration. According to Lugaro,²⁰ "Degeneration is a disturbance of physiologic hereditary transmission it is a disease of the hereditary mechanism." The cause of degeneration is something external acting on the organism, and this factor may vary in successive generations. Degeneration therefore is a result of disease of the stock, but a disease that may be curable. If that is true, and the evidence furnished by the above cases seems to confirm such a view, it is of great importance that it be generally recognized.

¹⁹ Beitrag zur Lehre von den Hereditären Schnervenleiden, Hamburg, 1900.

²⁰ Trans. by Orr and Rows, Modern Problems in Psychiatry, Manchester, 1909.

TWO INSTANCES OF CHRONIC FAMILY JAUNDICE.¹

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Under the J. Alison Scott Research Fund.)

IN June, 1910, Tileston and Griffin,¹ of New Haven, published a report of four families in which this disease appeared in several members of each family. They presented a thorough review of the bibliography of the subject, the major part of which came from the French, though in both the German and English medical literature the condition was by no means ignored. I will take the liberty of giving a short *resume* of their work before presenting my own cases:

Basing their opinions upon their own cases as well as upon those of foreign authors, they conclude that the following points are characteristic of the disease: That it is a chronic, non-obstructive jaundice, with enlargement of the spleen, occurring usually in hereditary form, or in several members of one family, and dating from birth, or first being noticed during adolescence. The icterus is not intense, there are no signs of obstruction of the bile ducts, and symptoms of cholemia, such as itching, xanthemas, and multiple hemorrhages, are lacking. Enlargement of the spleen is almost a constant feature, while enlargement of the liver is unusual.

"Bilious attacks" are extremely common, especially in youth. Headache, diarrhea, and slight fever are occasionally noted. After a day or two the attack passes off, to recur several times in a year. Gall-stone colic is frequently associated, as is, less often, perisplenitis. No hemorrhages are encountered other than epistaxis, which is not uncommon. The jaundice is pronounced in the conjunctiva and the skin of the body is yellow, while the face is of a peculiar characteristic buff color, varying in intensity from time to time, fatigue and worry tending to increase it.

The urine is highly colored, urobilin is present in the majority of cases, as is also urobilinogen, while bile is almost always absent. Urochrome is constantly increased, which accounts for high coloring.

The stools are well-colored, and urobilin and bile are always present, giving marked reactions to corrosive sublimate and Schlesinger's test. Moller has shown the total urobilin excretion in urine and feces to be considerably increased. Constipation is often present.

¹ Read before the Pathological Society of Philadelphia, January 23, 1913.

² AMER. JOUR. MED. SCI., June, 1910.

The blood-serum always shows the presence of bile-pigment, but not of urobilin. The important feature which gives a clue to the nature of the disease is the decreased resistance of the red blood cells to hemolyzing agents, that is, the increased fragility, which was first discovered by Chauffard. The method for testing for it is as follows: The red blood cells are separated from the plasma, washed, and then placed in a series of test-tubes in which are varying strengths of hypotonic salt solutions, varying from 0.7 per cent. down to 0.36 per cent. NaCl. In normal blood, hemolysis starts at 0.44 per cent., while in this disease it starts almost always at some point higher and not infrequently at 0.6 per cent. or even 0.7 per cent. This marked decrease in resistance is all the more important, because in chronic obstructive jaundice the resistance is normal or increased. Hemolysins have never been found in the blood-serum. A moderate anemia, with red counts between 3,000,000 and 4,000,000, is common. Abnormally high counts have been found. Color-index is usually normal. Average size of red cells is reduced. Reticulation of red cells as shown by the "vital" method of staining is apparently a constant feature. Nucleated red cells and anisocytosis are not rare. Leukocytes are normal.

PATHOLOGY. At autopsy liver appears normal, no obstruction of bile ducts, and no cirrhotic changes. Gallstones have been found several times. Spleen enlarged and shows evidences of old perisplenitis. Increase is in pulp, the trabeculæ being, as a rule, not much enlarged. Microscopically there is a marked engorgement, with blood, this being most evident in the pulp. The bone-marrow is found to be in a state of intense reaction.

ETIOLOGY. The red cells being more fragile, are readily destroyed, which leads to the anemia and in turn to an increase in free hemoglobin, out of which bile-pigment is made, and hence pleiochromia and icterus. Such a hemolytic icterus has been produced experimentally by Lesné and Ravaut by the injection of hemolytic agents, which is followed by jaundice, increase in size of spleen, and appearance of urobilin, bile, or hemoglobin in urine. Increased destruction of red cells probably takes place in the spleen, and hence its increase in size.

In conclusion, the following cases are presented:

Family No. I.

CASE I.—B. A. R., male, aged nineteen years; student. Came to the hospital complaining of yellow discoloration of skin. For three days the patient had noticed a gradually increasing jaundice; there had been no disturbance of digestion nor indiscretion of diet. Bowels were moderately constipated. There was no itching of the skin nor disturbance of vision or other symptoms due to jaundice, except a slow pulse, 58, which was soft and regular; appetite was fair; no fever.

Previous Medical History. Health was always good. Had had three or four attacks of jaundice a year as long as he could remember, but none so marked as this one. Had rheumatism three years before, otherwise negative.

Family History. Grandfather and father had had frequent attacks of jaundice and pain in the upper right abdomen. Sister had somewhat similar attacks, though milder.

Physical Examination. Slender young man of moderate nutrition. Oral mucous membrane pale; tonsils normal. The skin was of a deep yellow tinge; pigment was uniformly distributed over the body; sclera were deeply stained. Lungs and heart were normal. Liver was not palpable; flatness extended from the fifth interspace to the costal margin. The spleen, though not palpable, was considerably enlarged to percussion.

Blood-pressure: Systolic, 110; diastolic, 60. Urine was negative.

Blood Examinations: Hemoglobin, 65 per cent.; red cells, 300,000,000; leukocytes, 7600.

Feces: Clay-colored at beginning of attack for one day, at other times were brown. Occult blood was negative.

Fragility Test: Increased from 0.44 per cent. normal to 0.6 per cent. saline.

Patient's condition remained stationary for five days, after which the jaundice began to clear up. Temperature reached 100° for one day, and then remained normal to subnormal. Pulse rate, 50 to 60. Ten days later he returned for a blood analysis. There was no increase in fragility of erythrocytes at that time. Blood-serum was still greenish yellow, and showed strong bile bands in the spectrum. General condition was much improved, but still showed some jaundice. Seven months later the blood-count was normal. Coagulation time was eight minutes. Fragility increased to 0.48 per cent. NaCl. Bile in the serum. Three months later he was readmitted to the hospital. A tinge of jaundice had remained over the whole of the body. Just previous to admission he was suddenly seized with cramp-like pain in the pit of the stomach, which doubled him up, but it passed away in five minutes. Examination at that time revealed an enlarged and readily palpable spleen and hepatic dulness extending 4 cm. below the ribs in the parasternal line. Stools were dark in color.

Blood Examination: Hemoglobin, 79 per cent; red cells, 3,820,000; leukocytes, 6900. There was some polychromatophilia, also slight anisocytosis and poikilocytosis; red cells were fragile and many were crenated.

Fragility: Hemolysis started at 0.48 per cent. NaCl and was complete at 0.42 per cent.

Serum: Spectroscope showed bile bands. Hemolytic to blood cells of six cases showing normal resistance, but did not affect cells from seven other cases.

CASE II.—N. J. R., father of Case I. Health when presented was good. Had always had a tendency to bilious attacks and headaches. As a boy these would come on after the slightest change in his daily routine, diet, or after any excitement. Attacks began with headache, followed by nausea and vomiting, constipation, and drowsiness for several days. Bowels were constipated, requiring cathartics each day. If they missed a day an attack of headache, etc., would result. After onset of attack, thorough evacuation or vomiting would often bring it to an end. For some years these attacks were followed by mild jaundice. Occasionally, and especially seven or eight years before, he had distinct jaundice. General health not especially affected. Had gained weight in last few years.

Past Medical History. Otherwise negative.

Family History: Father had a tendency to sallowness. Brothers and sisters had no similar trouble. Son had a distinct type of familial trouble. Daughter had slight signs of similar trouble.

Physical Examination. Had an anemic appearance. Eyes were a bit puffy. Slightly sallow complexion. There was no definite jaundice. Liver and spleen were not palpable. Urine and stools were normal. Blood examined for fragility showed normal resistance. Serum was hemolytic to two cases and negative to one.

I did not have an opportunity to examine personally the next two cases:

CASE III.—Grandfather of Case I.

Blood Examination: Red blood cells were fragile to 0.54 per cent. Serum was negative.

CASE IV.—Sister of Case I.

Blood Examination: Erythrocytes showed normal resistance. Serum showed no bile bands. Hemolytic to two cases.

Family No. II.

CASE V.—A. L., male, aged twenty-five years; single. No recent illness. Had diphtheria and measles in childhood. For years had been subject to "bilious attacks," three or four times a year. Was almost always slightly jaundiced, the sclera especially being jaundiced during the "bilious attacks." Had had several attacks of severe pain in gall-bladder region, which he believed to be due to gall-stones. Attacks were always worse in summer or when he was tired out or worried. Pulse was infrequent, often reaching a rate of 54.

Family History. Grandmother was always jaundiced. Father was jaundiced and had "bilious attacks" of the same type as the patient, which were much more frequent in his earlier years. Next to his oldest sister had attacks each month, unassociated with her menses; she was always moderately jaundiced. Stools were frequently clay-colored; urine was dark. General health was

never very good. The next two children were free from jaundice or "bilious attacks." The next three were always slightly jaundiced, and were subject to attacks similar to those of the patient. One had had two severe attacks of gall-stone colic.

Physical Examination. Examination of the patient showed that he had not had an attack for several months except from a slight icteroid hue of skin.

Blood: Hemoglobin, 100 per cent.; red cells, 5,200,000; leukocytes, 4700.

Serum was greenish yellow, and presented strong bile bands in spectroscope. Fragility of erythrocytes started at 0.48 per cent. NaCl. Urine was negative. Stools were dark brown.

A summary of the cases in these families was as follows: The jaundice was in every instance chronic, non-obstructive, and familial in type. In the first family, four members of which had had attacks of varying severity, it may be noted that it extended over three generations, and that the attacks were more frequent and more severe in youth. The spleen was enlarged in each attack, at which times there was a moderate degree of anemia.

Throughout the course of Case I, which we have been able to follow more closely than any of the others, it will be observed that the fragility of the red blood cells ran *pari passu* with the "bilious attacks" and the increase in intensity of jaundice.

Case II did not show any increase in fragility, nor did Case IV, both of which had been free of attacks for some time. Case III showed a lessened resistance of red cells up to 0.54 per cent. NaCl.

The second family presented interesting features, in that three generations were involved and no less than five children in one immediate family were subject to the condition at that time. Owing to the fact that most of the family were living in Canada and New England, I have been unable so far to carry out further studies on the individual cases.

In one point my findings do not confirm those of Tileston and Griffin, as I have found in the serum of three members of this group isohemolysins to be present in ten out of a series of nineteen experiments.

In conclusion, I wish to extend my thanks to Drs. Stengel and Arthur Landry for the opportunity of studying these cases.

CLINICAL AND METABOLIC STUDIES OF A CASE OF HYPOPITUITARISM DUE TO CYST OF THE HYPOPHYSIS WITH INFANTILISM OF THE LORAIN TYPE (SO-CALLED TYPUS FROEHLICH OR ADIPOSEO-GENITAL DYSTROPHY OF BARTELS).

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INTRODUCTION. Through the efforts of Cushing, Goetsch, and Jacobson considerable light has been thrown on our knowledge of the function of the pituitary gland, especially in its diseased states. Our biochemical knowledge of this gland is scanty, and most of the work conducted has been in relation to the study of the metabolism in animals after extirpation and in acromegaly.

Schiff¹ found no increase in the nitrogen of the urine in acromegaly, but did find an increase in the phosphorus of the feces. Moraczewski² found a retention of nitrogen, phosphorus, calcium, magnesium, and chlorine in acromegaly. Oswald³ found that feeding pituitary extract to a dog had no effect on the nitrogen or phosphorus. Thompson and Johnson⁴ found that pituitary substance stimulates metabolism in the dog to an increased degree, as shown by the output of nitrogen, urea, and phosphorus in the urine and also in the decline of the body weight.

Malcolm⁵ found that the fresh whole gland increased the output of nitrogen. Benedict and Homans⁶ found that the removal of the pituitary gland of dogs produced a tendency to retard the normal growth of the animal and a marked fall of the total metabolism as measured by the carbon-dioxide production. Aschner⁷ found that total hypophysectomy in dogs caused a falling off in the nitrogen metabolism and the total metabolism of the fasting animal. The relation of the pituitary body to carbohydrate tolerance has been carefully studied by Goetsch, Cushing, and Jacobson.⁸ Von Narbut and others in v. Bechterew's laboratory observed after hypophysectomy a diminution in the carbon-dioxide output, slight diminution in the oxygen intake, an enormous loss of water,

¹ Wien. klin. Woch., 1897, x, 277; Zeitsch. f. klin. Med., 1897, xxxii, Suppl., p. 289.

² Zeitsch. klin. Med., 1901, xliii, 336.

³ Jour. Phys., 1905, xxxiii, 189.

⁴ Jour. Med. Research, 1912, xxv, 409.

⁵ Wien. klin. Woch., 1909, xxii, 1730; Verhand. d. Deutsch. Gesell. f. Chir., 1910, xxxix, 46.

⁶ Johns Hopkins Hosp. Bull., 1911, xxii, 165.

⁷ Virchow's Archiv, 1902, clxix, 44.

⁸ Ibid., 1904, xxx, 270.

and marked increase in the excretion of nitrogen and phosphorus. Wolf and Sachs⁹ found after extirpation of part of the anterior lobe and all of the posterior lobe a distinct lowering of the carbon-dioxide output, and after removal of the anterior lobe only a lowered carbon-dioxide output, while after complete hypophysectomy they found a marked decrease in the carbon-dioxide output and an unusually low nitrogen output.

Edsall and Miller¹⁰ noted a retention of nitrogen and phosphorus in two patients with acromegaly. Franchini¹¹ found a retention of nitrogen, calcium, and magnesium in a patient with acromegaly; while the sulphur, chlorine, and phosphorus metabolism was normal. Mendel¹² also found a retention of nitrogen and a change in chlorine and phosphorus metabolism. Tauszk and Vas¹³ found a slight retention of nitrogen and phosphorus and an increased calcium output. On giving pituitary tablets, no influence was exerted on the general metabolism.

Oberndorfer¹⁴ after careful observations on a patient with acromegaly formed no definite conclusion regarding the character of the metabolism, and was inclined to doubt the finding of definite abnormalities of metabolism in acromegaly. Franchini¹⁵ found extracts of pituitary body of cattle and horse caused a marked loss of calcium, magnesium and phosphorus excretion when injected intravenously into rabbits and guinea-pigs. Mochi¹⁶ found that the subcutaneous injection of pituitary gland caused in rabbits a slight loss of nitrogen and a marked loss of calcium and phosphorus. Medigreceanu and Kristeller¹⁷ studied the general metabolism, with special reference to the mineral metabolism in a patient suffering from acromegaly complicated with glycosuria, and found that the glycosuria followed the usual course of this symptom, while the carbohydrate tolerance was in no way affected by injections of the extract of the anterior lobe of the hypophysis, there was noted a general rise of metabolism after the injection. There also resulted from the injection peculiarities in salt metabolism which could not be interpreted on the basis of the rise of the general metabolism.

None of the experimental work that has been conducted on the question of metabolism in perversions of the pituitary gland can be compared with the study we describe in this paper. As may be noted in the case report, the patient is a classical type of hypopituitarism the opposite of acromegaly (hyperpituitarism), the condition which has been the subject of the several metabolic studies mentioned before.

⁹ Proc. Soc. Expt. Biol. and Med., 1910, viii, 36.

¹⁰ Univ. of Penna. Med. Bull., 1903, xvi, 143.

¹² Deutsch. med. Woch., 1906, p. 1975.

¹⁴ Zeitsch. f. klin. Med., 1908, lxx, 6.

¹⁵ Berl. klin. Woch., 1910, pp. 613, 670, 719.

¹⁶ Riv. di patol. nerv. e ment., 1910, xv, 457.

¹⁷ Jour. Biol. Chem., 1911, ix, 109.

¹¹ Bioch. Zentral., 1905, p. 522.

¹³ Jahr. f. Neurol., 1899.

CLINICAL DATA. Hypopituitarism due to cyst of the hypophysis, with progressive bitemporal hemianopsia leading to optic atrophy and infantilism of the Lorain type (so-called *typus Froehlich* or *adiposo-genital dystrophy of Bartels*). Kanavel operation.

B. S., male, aged twenty-two years, native of Hungary, unmarried, was admitted to the surgical service of the German Hospital, New York, February 3, 1912.

Family History. The patient has three brothers and three sisters. They are all alive and well, and the men are above the average height. No other member of the family is afflicted in the same manner as the patient. There is no history of consanguinity, alcoholism, lues, tuberculosis, or cancer.

Previous History. The patient had measles and chicken-pox when a child.

Present Illness. When the patient was about ten years old it was noticed that he was not growing normally. Up to this time he had suffered from enuresis, which ceased at his eleventh year. He also began to complain of headaches, which were so severe that they prevented him from playing with other children, and even kept him awake at nights. His eyes watered considerably, and when he was thirteen years old it was discovered that his sight was so poor that he could no read the blackboard at school. Since then his eyesight has been gradually getting worse, so that now he is practically blind. His headaches have continued, and are dull and frontal in character. His physical development has been greatly retarded. He is very irritable. There has never been any indication of sexual power, neither libido, erection, nor ejaculation. There has never been nausea nor vomiting, dizziness, vertigo, loss of consciousness, nor convulsions. He has never shaved. Appetite is poor. Bowels are constipated. Micturition: diurnal 3, nocturnal 1. No polyuria. Some polydipsia. Chief complaints, blindness, headache, arrested development.

Status Praesens. General (Figs. 1 and 2): The patient is a much underdeveloped, but not poorly nourished male. He is 137 cm. ($4\frac{1}{2}$ feet) tall and weighs sixty-six pounds. His size is about that of a child of nine or ten years of age. He is somewhat pale and sallow, and his skin is dry. There are no eruptions nor adenopathies. There is a moderate adiposity. The mentality is sluggish, but the patient is not unintelligent nor illogical. There is no trace of imbecility. He talks little, but answers intelligently. The hair on his head is normal, but the patient has not the trace of a beard nor moustache, and no pubic nor axillary hair.

Head: The nose, mouth and pharynx are normal. The ears are rather large, but the hearing is normal. The head measures 55 cm. in circumference. The olfactory nerves are normal, as are all the other cranial nerves, with the exception of the optic. The teeth are in fair condition, and with the exception of the third molars have all erupted. The thyroid is small.

Eyes: The right eye is totally blind. With the left eye the patient can count fingers at one foot. The visual field, however, is much contracted, the temporal half being entirely absent. The pupils are of equal size and are large. There is no consensual nor direct reaction to light from the right eye. In the left eye both reactions are normal. The reaction is much more prompt and

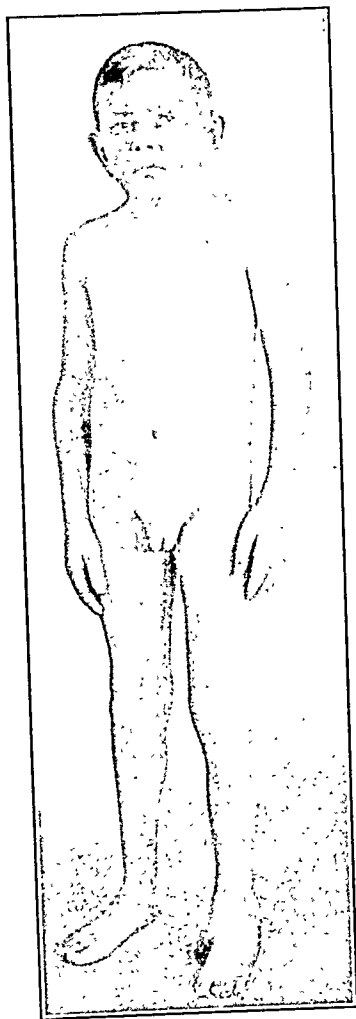


FIG. 1.—Note infantile genitals and absence of facial and pubic hair. Taken before operation.



FIG. 2.—Taken nine months after operation. Orderly is of average height, five feet eleven inches. Note absence of facial deformity from operation.

effectual from the nasal side. The refractive media of both eyes are clear. The disk of the right eye is white and the retinal vessels are well defined. The ophthalmoscopic examination of the left eye gives much the same picture. Diagnosis by Dr. Schirmer: primary optic atrophy.

Chest: Small, round, symmetrical. No deformities. No enlargement of thymus.

Lungs: Breathing over left lung normal. Rather harsh breathing, with slightly increased vocal fremitus and slight dulness over the middle lobe of the right lung. Over the upper lobe, posteriorly, on the right side a few crepitant rales may be heard.

Heart: Apex sounds normal. Aortic second somewhat accentuated. Heart action regular, percussion normal.

Abdomen: Soft, symmetrical. No abnormal masses, no areas of tenderness nor rigidity.

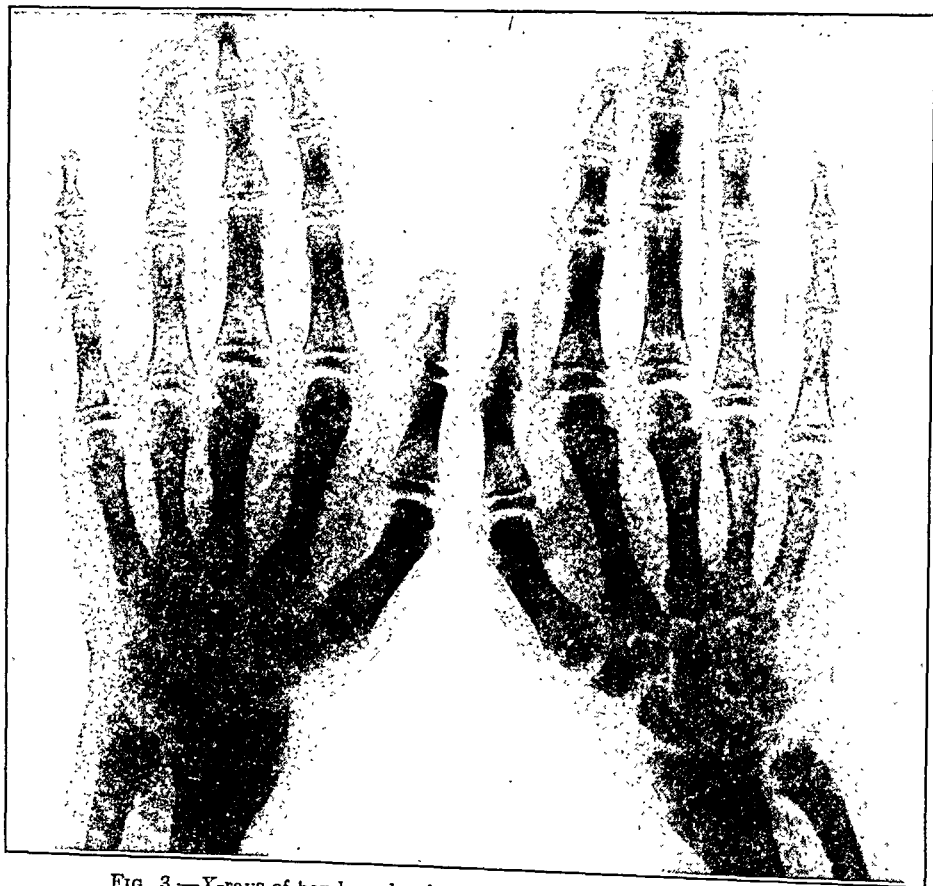


FIG. 3.—X-rays of hands and wrists, showing marked arrest of ossification.

Extremities: Hands and feet are small and delicately formed. The fingers are tapering; the nails are well formed, but there are no crescents. The knee-jerks are sluggish. X-rays of hand (Fig. 3): The pisiform bones are missing and there are no sesamoid bones. The epiphyses of the phalanges, metacarpals, radius, and ulna are just beginning to unite. The ossification of the bones of the hand corresponds about to that of a boy eleven or twelve years old.

Genital Organs: The penis is small, and the testicles, though present in the scrotum, are exceedingly undeveloped. They measure about 1 cm. in their long diameter. There are no hernias.

Nervous System: Aside from the above-described condition of the eyes there are no abnormalities of the nervous system.

Measurements: From umbilicus to crown, 51 cm.; From umbilicus to soles, 86 cm.; from umbilicus to external malleolus, 77.5 cm., both equal; arms, 22.5 cm., both equal; forearms, 18.5 cm., both equal; from anterior superior spine to internal malleolus, 73.5 cm., both equal; from ulnar styloid to tip of little finger, 14.5 cm., both equal.

Temperature, 99°; pulse, 112, soft and regular; respiration, 24. Blood pressure, 70 mm. of mercury.

Urine: 1260 c.c., acid; amber; clear; specific gravity, 1022; no protein; no sugar. The carbohydrate tolerance is greatly increased, the patient taking as much as 400 grams of glucose without sugar appearing in the urine.

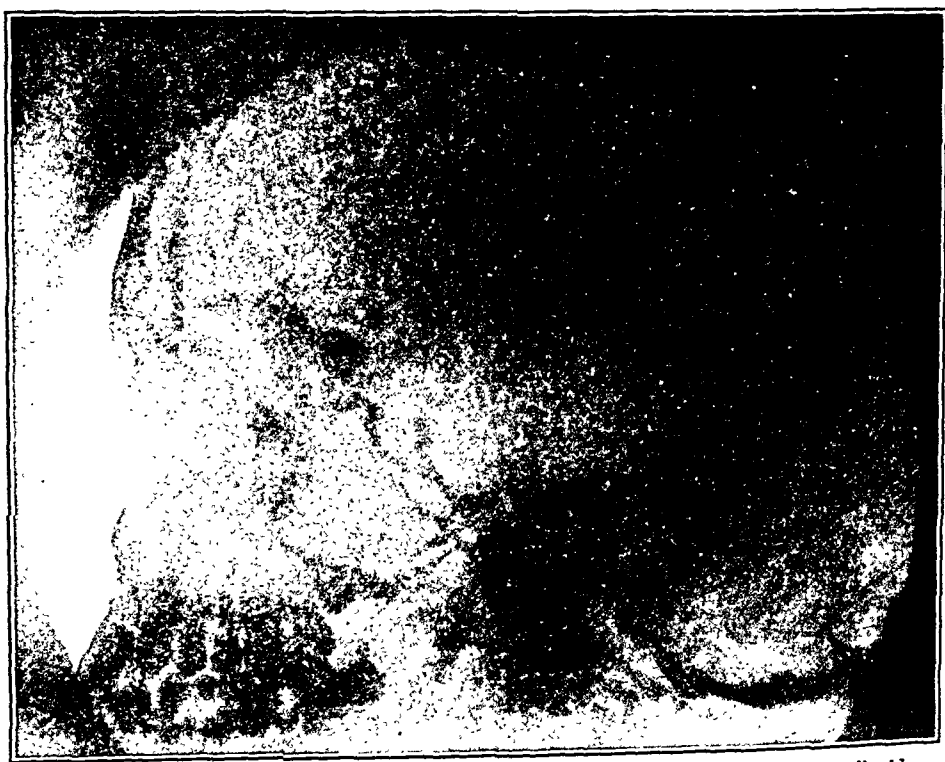


FIG. 4.—X-ray of skull, showing erosion of dorsum of sella turcica and posterior clinoid processes.

Blood count: Red corpuscles, 3,900,000; hemoglobin, 55 per cent.; white corpuscles, 10,000; polynuclears, 65 per cent.; large lymphocytes, 1 per cent.; small lymphocytes, 28 per cent.; mononuclears, 5 per cent.; eosinophiles 1 per cent.

The Wassermann reaction is negative.

X-ray examination of the skull (Fig. 4) shows an erosion of the dorsum of the sella turcica and of the posterior clinoid processes.

There also seems to be an erosion of the posterior wall of the sphenoidal sinus.

We have here a classic case of infantilism of the Lorain type, with symptoms definitely pointing to a benign tumor, probably a cyst of the hypophysis. The general pressure symptom of headache and the distinct neighborhood signs—namely, the primary optic atrophy, apparently beginning as a bitemporal hemianopsia, and the x-ray picture of the skull—made this rather clear. We were obviously dealing with an exquisite case of hypopituitarism beginning in early life. The arrest of body growth and of sexual development, with the moderate adiposity, stamped this case as a typical example of the Froehlich typus or the so-called dystrophia adiposo-genitalis of Bartels. The glandular symptoms are, in the main, due to a deficiency of the anterior lobe of the pituitary gland, although it is evident that the posterior lobe function is also diminished, as indicated, by the high carbohydrate tolerance and the unusually low blood pressure.

In the hope of improving the eyesight and avoiding the threatened total blindness, and incidentally relieving the headaches, operation was decided upon.

Urotropin given and nasal cavity irrigated as a preliminary measure. February 21, 1912, operation by Dr. F. Kammerer. Preliminary inferior tracheotomy. Thyroid gland apparently normal. Ether anesthesia through tracheotomy opening. Pharynx packed with gauze through mouth.

Kanavel's infranasal sublabial trans-sphenoidal approach. A transverse incision was made at the reflexion of the mucous membrane of the upper lip on the alveolar process. The tissues were then elevated and the nasal cavity entered. The cartilage of the septum was incised anteroposteriorly at its junction with the palatal process of the superior maxilla. The cartilage was not removed. The nose was retracted upward. Both inferior and middle turbinates, vomer, and vertical plate of the ethmoid were removed with a rongeur. The bleeding, which was remarkably insignificant, was easily controlled by adrenalin tampons. The anterior wall of the sphenoidal sinus was now clearly seen and removed. The exposure was excellent and there was ample room. As soon as the sinus was opened there was a gush of about an ounce of turbid serous fluid. This was obviously the contents of a cyst, which had eroded the posterior wall of the cell. The fluid was clearly not from the cerebrospinal cavity, as the discharge ceased promptly after it was mopped up and the pulsating dura was seen intact in the depths of the wound.

It was now decided that it would be inadvisable to do anything further as the chief object of the operation had been accomplished namely, the relief of pressure on the chiasm. The cavity was packed with two small iodoform tampons, one of which was led

out through each nostril. The sublabial incision was carefully sutured with silk.

The fluid from the cyst was sterile. It was not possible to obtain sufficient material for proper cytological or chemical examination.

February 23. Tampons removed from nose.

February 24. Tracheotomy tube removed.

February 25. Irrigation of nasal cavity with saline started.

The patient stood the operation well and reacted promptly. Twenty-four hours after operation the temperature rose to 103° ; with pulse of 110, and remained so for five days. Then the temperature and pulse gradually came down, but again rose on the ninth day. From this time there were irregular rises and falls of temperature from 103.5° to 100° for nine weeks following the operation. The patient was drowsy, slept most of the time, ate very little, vomited frequently, complained of headache, looked pale, and began to get edema of the face, hands, and feet. He was put on large doses of urotropin.

In spite of constant irrigation of the nasal cavities there was a profuse purulent discharge, especially from the right side. There was no rigidity of the neck, no increased reflexes, and no Kernig symptom.

March 3. Anterior lobe, desiccated pituitary substance, grain j, given three times daily. Discontinued March 8.

April 4. Spinal puncture. 5 c.c. of clear fluid withdrawn. No pressure. Report of Dr. Garbat: No fibrin filament on standing. Very scant sediment after centrifuging. Few cells, but insufficient in number for differential count. Few Gram positive cocci. Globulin reaction negative. Acetic acid test plus. Reduction of Fehling's faint. Cultures: Plate directly from fluid, sterile. Broth tubes from fluid show *Staphylococcus albus*, evidently a contamination.

The temperature remained high and the symptoms about the same for a week following the spinal puncture. The case made an unfavorable impression, and there seemed little chance of a recovery. Then the purulent discharge from the nose stopped; the temperature dropped to normal and remained so; the headache disappeared; the drowsiness cleared up; the vomiting ceased, and the appetite improved. From this point the patient made a rapid recovery. There had evidently been an extradural suppuration at the site of the old sphenoidal sinus, and this chronic suppurative process, which had been responsible for the septic and pseudo-meningitic symptoms, had now healed.

The eyesight, however, had not improved. If anything it was worse than before the operation. There was practically total blindness. There was perhaps a perception of light in the left eye. No pupillary reaction to light.

June 5. Ophthalmoscopic examination by Dr. Denig showed

optic atrophy of both eyes. The outlines of the disks were sharp, the veins normal, and the arteries a trifle narrow.

The wound in the mouth healed so well that the scar can scarcely be found. There is the slightest trace of a saddle nose as the only external evidence that an operation has been performed. Nasal examination shows a large perforation due to the absence of the bony septum. The turbinates are missing and the cartilaginous septum is deviated to the left. There is a slight serous discharge from the right side.

X-ray examination of the skull reveals no marked changes in the base of the skull.

July 2. The patient was discharged from the hospital, with headaches cured.

He has improved greatly since he left the hospital. He has been examined several times since, the last time on November 20. On November 16, he was presented at the demonstration in the German Hospital to members of the Third Clinical Congress of Surgeons of North America. He looks well, has a good color, and has gained ten pounds in weight since the operation. His headaches are entirely gone and he sleeps through the night, something that he has not done in many years. His appetite is excellent. His bowels are also more regular. His mentality is more active and he is much more talkative. His disposition has changed for the better. He has entirely lost his irritability. As to the sight, there does not seem to be much objective change, though the patient and his mother think there has been some improvement. He claims to be able to see quite well at times. He is able to walk alone on the street, and insists that he sees his way and does not feel it. He claims to see better at dusk. An examination of the eyes by Dr. Schirmer shows that the ophthalmoscopic picture has not changed. The right eye is blind and there is no pupillary reaction. With the left eye the patient can see movements of the hand and the pupil reacts normally. The nose is entirely healed and there is no more discharge. There has been no evidence of growth since the operation. The x-ray of the hand shows exactly the same condition as before.

The patient has been put on desiccated pituitary substance (anterior lobe), grains ij, three times a day, after meals.

METABOLIC DATA. *Methods.* Nitrogen determinations were made by the Kjeldahl method, the ammonia by the Folin method, urea by Benedict's new method,¹⁸ uric acid by the Folin-Shaffer method, total sulphur by Benedict's method;¹⁹ creatinin by Folin's method, total sulphates by Folin's method, inorganic sulphates by Folin's method. The ethereal sulphates were estimated by subtracting the inorganic sulphates from the total sulphates and neutral sulphur by subtracting the total sulphate-sulphur from the total sulphur.

¹⁸ Jour. Biol. Chem., 1910, viii, 405.

¹⁹ Ibid., 1909, vi, 363.

Samples of milk used in the diet were analyzed for nitrogen and fat. The nitrogen of the weighed eggs (minus shell) was computed with the aid of the figure given by Koenig (2.008 per cent. nitrogen). The feces were marked off by means of carmine into periods of three days. The fat content of the feces was determined by the method of Kumagawa and Suto.²⁰

The patient was placed on Folin's diet,²¹ consisting of:

Whole milk	500 c.c.
Cream (18 to 22 per cent. fat)	300 c.c.
Eggs (whole)	450 gm.
Horlick's malted milk	200 gm.
Sugar	20 gm.
Sodium chloride	6 gm.
Water	2100 c.c.

This diet contains approximately 119 gm. protein, 148 gm. fat, 225 gm. carbohydrate, yielding 2787 calories.

The following tables contain the results obtained in this study, and it may readily be noted that the absorption of protein and fat was normal in this individual, while the proportion of nitrogen of the urine as undetermined nitrogen and the proportion of sulphur of the urine as neutral sulphur are regularly much higher than the normal.

TABLE I.—(Nitrogen Partition) Urine.

Date.	Total nitrogen grams.	Urea nitrogen.		Ammonia nitrogen.		Creatinin nitrogen.			Uric acid nitrogen.		Undeter- mined nitrogen.	
		Grams.	Per cent. of total nitrogen.	Grams.	Per cent. of total nitrogen.	Grams.	Per cent. of total nitrogen.	Co-efficient. Milligrams.	Grams.	Per cent. of total nitrogen.	Grams.	Per cent. of total nitrogen.
June 23	13.0											
June 26	16.1	13.5	83.8	0.36	2.3	0.60	3.8	20	0.20	1.4	1.4	8.7
June 27	16.3	13.3	81.6	0.41	2.5	0.58	3.5	19+	0.24	1.5	1.6	11.0
June 28	15.7	12.6	80.3	0.40	2.5	0.56	3.5	18+	0.26	1.7	1.9	12.1
June 29	15.8	12.9	81.7	0.44	2.7	0.54	3.4	18	0.23	1.5	1.7	10.6
June 30	15.3	12.3	80.5	0.40	2.6	0.50	3.3	16+	0.27	1.7	1.8	11.7
July 1	15.7	12.6	80.2	0.48	3.1	0.55	3.5	18+	0.29	1.9	1.8	11.5

TABLE II.—(Sulphur Partition) Urine.

Date.	Total sulphur grams.	Total sulphate sulphur, grams.	Etheral sul- phate sulphur, grams.	Inorganic sul- phate sulphur, grams.	Neutral sul- phur, grams.	Sulphate sul- phur. Total sul- phur. Per cent.	Etheral sul- phate sulphur. Total sulphur. Per cent.	Inorganic sul- phate sulphur. Total sulphur. Per cent.	Neutral sulphur. Total sulphur. Per cent.
June 23	0.57	0.45	0.04	0.41	0.12	78.6	6.8	71.8	21.3
June 26	0.41	0.39	0.03	0.27	0.11	72.5	7.2	65.3	27.4
June 27	0.80	0.66	0.06	0.60	0.14	82.4	7.1	75.3	17.5
June 28	0.90	0.69	0.04	0.65	0.21	76.7	4.3	72.4	23.3
June 29	0.90	0.69	0.05	0.64	0.21	76.7	5.5	71.1	23.3
June 30	0.87	0.53	0.05	0.48	0.34	61.7	6.4	55.3	38.3
July 1	0.96	0.66	0.04	0.63	0.30	69.2	4.0	65.2	30.8

²⁰ Biochem. Zeit., 1908, v. 212.

²¹ Amer. Jour. Physiol., 1905, xiii, 45.

TABLE III.—Summary of Data Pertaining to Total Nitrogen and Fat Metabolism.

Date.	Total nitrogen.			Feces.			Fat.	
	Ingested grams.	Excreted grams.	Balance grams.	Fat grams.	Total nitrogen.		Ingested grams.	Absorbed grams.
					Found grams.	Per cent. of total nitrogen ingested.		
June 26 . . .	18.2	17.9	+0.3	2.2	1.8	9.9	140.0	137.8
June 27 . . .	18.6	18.1	+0.5	2.2	1.8	9.7	140.0	137.8
June 28 . . .	18.3	17.5	+0.8	2.2	1.8	9.9	140.0	137.8
June 29 . . .	18.1	17.9	+0.2	1.8	2.1	11.6	146.0	144.2
June 30 . . .	17.6	17.4	+0.2	1.8	2.1	11.9	146.0	144.2
July 1 . . .	17.8	17.8	0.0	1.8	2.1	11.9	146.0	144.2
Total	108.6	106.6	+2.0	12.0	11.7	858.0	846.0
Average	18.1	17.7+	+0.33	2.0	1.95	10.8	143.0	141.0

DISCUSSION OF METABOLISM RESULTS. During the six days on the standard diet it may be noted that the patient showed a slight retention of nitrogen, while the absorption of fat and protein was normal in degree. The percentage of the various urinary constituents were normal, with the exception of the neutral sulphur and undetermined nitrogen. The undetermined nitrogen of the urine is made up of substances present in variable amount and difficult to estimate. In this fraction are present various mono-amino and diamino-acids, hippuric acid, oxyproteic and alloxypoteic acids, allantoin and possibly other substances not yet defined. On a diet yielding about 16 grams of total nitrogen in the urine, Folin has shown that the undetermined nitrogen of normal urine is about 4 per cent. of the total nitrogen. The nature of the neutral sulphur of the urine is also uncertain; it may be made up of the sulphocyanates from the saliva, hydrogen sulphide, cystein, an intermediary compound of normal protein metabolism and taurocarbamic acid from bile. Traces of chondroitin-sulphuric acid and, oxyproteic acids also help make up the neutral sulphur content of the urine. Cystin, if present, would also increase the neutral sulphur. Folin has shown that the neutral sulphur of the urine is made up of substances, which in the main are independent of the total amount of sulphur eliminated or of protein catabolized and variations in the neutral sulphur of the urine, must be regarded as showing presence of abnormal metabolic processes, which are not associated with variations in the other types of urinary sulphur. On the diet given to this patient the neutral sulphur should not normally be higher than 10 to 12 per cent. of the total urinary sulphur.

We therefore have in this case a marked perversion of some metabolic process leading to high and abnormal percentages of the neutral sulphur and undetermined nitrogen of the urine. Our knowledge of these two groups of substances is very meager, and it would be unwise at present to attempt any specific explanation of this anomaly.

THE DIAGNOSIS OF GASTRIC ULCER.¹

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ULCER of the stomach is only diagnosticated about one-third as often as it should be. This has been proved at autopsy time and again, and can be shown clinically when routine employment of the more exact methods for the recognition of ulcer is tried.

In Cabot's report of the analysis of 3000 cases coming to autopsy at the Massachusetts General Hospital, he claims that but 36 per cent. of the ulcers of the stomach were correctly diagnosticated. It should be remembered, too, that this represents work of men who are well up at the head of the internists of the country.

Something is wrong. What is it? Are the means at our command for the diagnosis of ulcer inadequate? The writer thinks not. He believes that at least 90 per cent. of the cases should be recognized with our present diagnostic methods though the remainder will probably continue to baffle us.

There are several reasons for the great number of ulcers escaping detection. The average physician does not suspect the enormous number of dyspeptics the cause of whose trouble lies in ulcer of the stomach or duodenum. He looks for the former text-book symptoms and does not find them. The entire subject should be and will be rewritten.

Germany, feeling the need for more exact knowledge concerning ulcer, has appointed a committee of leading clinicians to investigate principally the etiology, and a subcommittee has been appointed in this country, but as they accept for their records only those cases which have been proved by operation or autopsy, the great mass of cases, the ones in fact that are the most difficult of diagnosis, will not be included, and we will be helped in the problem but little.

The real signs of ulcer are not tested for often enough in patients who have not the unmistakable ear-marks of ulcer. We want early diagnoses before the typical and evident symptoms appear.

It is generally accepted that there is an acute or so-called medical ulcer and the chronic indurated ulcer. There can be little doubt that there is at least a third class, chronic non-indurated ulcer, perhaps an intermediary stage or a forerunner of the indurated ulcer. Such a condition may persist for years and not be recognized. The average duration of the cases operated upon by the Mayos has been twelve and one-half years. Where have these patients been during all this time? Again the writer wishes to

¹Read at Symposium on Gastric Ulcer, joint meeting of Medical Societies of Georgetown University and George Washington University, January 11, 1913.

emphasize the importance of the early diagnosis at the very beginning of this long stretch.

The writer will not consider differential diagnosis because of lack of space. Indeed, it is not necessary if one bears in mind the diagnostic points of ulcer itself and remembers that another trouble may be present at the same time. For instance, if a patient undoubtedly has gallstones he may also have ulcer, since the two conditions are often concomitant.

The means at our command for the diagnosis of ulcer come under four headings: (1) Consideration of the history and symptomatology; (2) physical examination; (3) special tests and laboratory aids; (4) the therapeutic test.

HISTORY AND SYMPTOMATOLOGY. The history and symptoms complained of by the patient are typical in but few cases, notably, the chronic surgical ulcers and some of the acute ulcers. Most symptoms may be simulated by other conditions, and on the other hand for every ulcer with characteristic symptoms there are probably a couple of others with few if any of the symptoms which might be expected.

Pain may or may not be present. There is no characteristic sort of pain in ulcer. Perhaps the variety of pain which will be less apt to mislead than any other is that running through from front to back, expressed by patients "as if a stick were run through the body and then twisted around." This particular sort of pain is of some diagnostic importance, but in comparison with the whole number of ulcer cases is met with but rarely. It may be said that there are only two characteristic points about the pain in ulcer: its time of occurrence and the method of its relief. The pain appears at a fixed time after meals, different in different individuals, but always the same in the one patient. The pain is relieved by more food, alkalies, or vomiting.

Various acid symptoms of heart burn, pyrosis, regurgitation, etc., are all common in ulcer, and doubtless many of the "sour stomachs" if studied closer would be found to be due to ulcer, but these symptoms are by no means characteristic of ulcer.

Hematemesis, one of the old cardinal symptoms, probably does not occur in 10 per cent. of the patients. As Cabot remarks, it is decidedly more characteristic of cirrhosis of the liver than of ulcer.

Even nausea and vomiting, while undoubtedly present many times, do not occur in one-half of the ulcer patients, and these symptoms even when present have absolutely no value unless it be in the effect of the vomiting in stopping pain.

There are two points, however, in the consideration of the history which are of decided value in the diagnosis of indurated ulcer. There is exhibited a certain periodicity in some of these cases. The patient may have been miserable for a couple of months,

when suddenly with no apparent reason and often in spite of some gross indiscretion he will be completely relieved of all symptoms and enjoy good health for a varying period of days, weeks, or months. These periods of euphoria and misery alternate to the patient's complete mistification, and in stating their history he will frequently comment on this with expressions of surprise.

The other important point is that when pain is at its height all other symptoms from which the patient is suffering are apt to be increased also, and that they tend to be relieved by the same measures which stop the pain.

It is surprising how frequent are the mistakes even in these chronic ulcers, the easiest of any to diagnosticate, simply because the physician still looks for pain, vomiting, and hematemesis, and overlooks the periodicity of symptoms and the manner of their relief. Within the past month the writer saw two chronic ulcers, one of twelve years' duration and the other of seven years. The diagnosis was easy in both cases after talking with the patients for about five minutes, and was corroborated by tests and later by operation, and yet one of these patients had consulted several physicians and had been under observation in the ward of one of the city hospitals for three weeks, while the other had in the course of the twelve years consulted as many physicians and only one of the number had ever suggested ulcer, a surgeon in Denver.

PHYSICAL EXAMINATION. The results of physical examination are, on the whole, somewhat more reliable than the consideration of the history and symptoms.

There is usually present at some time a tender point at some spot in the epigastrium or at the eighth dorsal vertebra behind, or both. The tenderness is often slight and is at times absent. In order to be of diagnostic value the tenderness should always be in the same place, and there should be but one spot. Points of marked tenderness can often be found in enteroptotic nervous women, but usually further examination will reveal that there are several of these spots.

Muscle spasm and rigidity are, when present, but further evidence of tenderness.

SPECIAL TESTS AND LABORATORY AIDS. The special tests and laboratory aids afford us the most exact means of diagnosing ulcer. The writer attaches more importance to the test for occult blood than to any of the others. Occult bleeding occurs in the large majority of all ulcers regardless of the duration or variety. The bleeding is, however, characteristically intermittent, and for that reason several examinations under varying conditions should be made. The benzidine reaction is the best of which the writer has knowledge. Being as delicate as it is, several precautions are necessary. Test-tubes should be absolutely clean. The patient may be on regular diet when the first examination is made,

but if a positive test is secured he should then be put on a meat-free diet for several days, to exclude the blood from the meat and the test repeated. If a positive test is then obtained, all bleeding points, as hemorrhoids, bleeding gums, etc., should be excluded. If negative results are obtained in a case which has a suspicion of ulcer the patient should be placed upon a coarse and irritating cellulose but meat-free diet for a couple of days. The writer never feels certain of a diagnosis of ulcer without the presence of occult bleeding.

Hyperacidity is found in a large proportion of all patients with ulcer, but is not to be compared in value to the presence of hypersecretion, which is a valuable indication, though not by any means pathognomonic of ulceration.

Meunier rinses the stomach out with 1 per cent. acetic acid solution and tests the rinse water for blood. This procedure has been of service to the writer in several cases, but it is an admitted fact that the test for occult blood in the stomach contents has not the same value as for that in the stool. The tube itself is too apt to produce small abrasions of the mucosa.

The x -rays are of undoubted value in the diagnosis of ulcer, and may be necessary in some doubtful cases, but has several manifest disadvantages. It is an expensive procedure and the average patient cannot afford it. Not only is it sometimes impossible to get pictures taken, except in the largest cities, but the interpretation of the findings requires the services of an expert of considerable experience in stomach x -ray work.

One of the latest and most ingenious methods which has been devised for the diagnosis of ulcer of the stomach and duodenum is the thread-impregnation test of Einhorn. The writer has used this test from the time it was first described, and has had large experience with it, and yet even now holds it more or less *sub judice*. As a test for the localization of ulcer it is well-nigh perfect. As a means of diagnosis it has been the writer's experience that certain positive threads are almost infallible, but he does not believe that a stained thread always denotes ulcer even in the absence of cirrhosis and cancer.

The technique of the test has been already described several times by Einhorn, Morgan, and the writer, so that it will not be again given. It will suffice to say that a silk thread, swallowed at night by the patient and retained all night, rubs to and fro against the ulcer and causes it to ooze blood so that a stain is left on the thread and is plainly visible when the thread is pulled up in the morning.

The writer has found that those threads with a plain mark or two marks denoting the rim of an ulcer, with an unstained portion between, are never misleading. Again, any sort of a stain which is present on two or more threads at exactly the same point is a sure

indication of ulcer. On the other hand, the writer cannot believe that the many instances of diffuse stained thread are all caused by ulceration. A stained thread, however, always does denote a pathologic condition of the mucous membrane, if not ulceration, then a soft, spongy state. It is probably these same cases which often have the wash water from lavage returned red with blood, simply from the irritation of the tube, when we can be almost sure that no ulcer is present.

THERAPEUTIC TEST. Some cases will continue to defy our ability to make a diagnosis, and these will have to be treated as ulcers and the results of treatment noted. The writer has treated some patients for weeks for other conditions, always bearing in mind the possibility of ulcer, while others he has treated as ulcer, on suspicion, never feeling sure as to the diagnosis, and has been rewarded by the therapeutic test confirming his suspicions.

In conclusion, there are several combinations which practically assure a diagnosis:

Tender point with occult blood.

Hypersecretion with tender point.

Hypersecretion with occult blood.

Tender point with repeated positive thread tests.

Tender point with hematemesis.

Hematemesis with hypersecretion.

Hypersecretion with positive thread tests.

REVIEWS

THE MODERN TREATMENT OF NERVOUS AND MENTAL DISEASES
BY AMERICAN AND BRITISH AUTHORS. Edited by WILLIAM A.
WHITE, M.D., Superintendent of the Government Hospital for the
Insane, Washington, D. C., Professor of Nervous and Mental
Diseases in the Georgetown University, and SMITH ELY JELLIFFE,
A.M., M.D., Ph.D., Adjunct Professor of Diseases of the Mind
and Nervous System in the Post-graduate Medical School and
Hospital, New York. 2 volumes; pp. 1630; illustrated.
Philadelphia and New York: Lea & Febiger, 1913.

THIS is indeed a modern "treatment." The family doctor has for years been asked to buy treatments of nervous and mental diseases, only to be confronted by the same old story of massage, electricity, hydrotherapy, and rest cures until he has associated these methods as the only ones which can possibly be employed for the cure of those who are unfortunate enough to come into the hands of a neurologist. It is therefore high time for this book. Indeed the authors are to be admired for their courage in presenting a work of this sort.

We have in these two volumes monographs by different men in this country and England which apparently have been edited. Rather an unusual feature in volumes by many authors. The subject matter has been well selected. The publishers have done their work well, although the illustrations leave much to be desired, not because those that are present are not good, but because there are not enough of them. To the reviewer, no book is complete without free illustrations, for it is the best way to teach anything.

Such unusual subjects are discussed as eugenics and heredity, educational and sexual problems, the feeble-minded and their treatment, delinquency, immigration, and the mixture of races, and then what is certainly very unusual, because these subjects have always been considered incurable, such diseases as dementia præcox, maniac depressive psychoses, paranoia and paranoid states, presenile conditions, and then nervous disorders occurring in prisons and in military duty. All this in the first volume.

The second volume contains the usual diseases of the nervous system. It is difficult to pick out any one chapter or any one subject for special mention because they are nearly all good.

What should be most highly praised is the selection of the subjects discussed, for, as is well said in the introduction, "this book begins where others leave off."

It is not at all, therefore, surprising in such a book as this that sexual problems are treated as if they really occurred in the human race, instead of apologizing for mentioning them. Not at all surprising is the fact that the neuroses are treated from the Freud standpoint and too much tabooed subject of psychoanalysis is adequately discussed. Neither is it surprising that in the discussion of insanity instead of fitting in all symptoms to certain diseases, a psychological standard is adopted. Altogether one finds a great deal of joy and hope in the future of neurology in such a work as this.

T. H. W.

LIFE AND LETTERS OF DR. WILLIAM BEAUMONT. By JESSE S. MYER, M.D., Associate in Medicine, Washington University. Pp. 317; 58 illustrations. St. Louis: C. V. Mosby Co., 1912.

THE story of Alexis St. Martin and Dr. Beaumont has always had a fascination for those who have heard only a fragment, but we are now in possession of a monumental work, which being read, must deepen our admiration for this American pioneer, and his remarkable physiological researches. The zeal with which Beaumont pursued his studies and his recreant and totally worthless subject, are told with a simplicity and directness whose reward is the strong appeal it makes. Dr. Myer deserves the highest commendation for his compilation and the difficulty of his undertaking can be appreciated by any one who will read his preface. The book is replete with suitable illustrations, and letters of Beaumont are preserved in their original form thereby giving an atmosphere to the book which is most entertaining. What a contrast the difficulty and primitiveness of Beaumont's researches and technique bear to the modern facilities for undertaking a physiological problem! We recommend to all this exceptionally good biography.

E. H. G.

A TEXT BOOK OF BIOLOGY. For students in medical, technical, and general courses. By WILLIAM MARTIN SMALLWOOD, Ph. D., (Harvard). Professor of Comparative Anatomy in the Liberal Arts College of Syracuse University. Pp. 285; 243 engravings and 13 plates. Philadelphia and New York: Lea & Febiger, 1913.

THIS book is one of the newer forms of texts in which the attempt is made to give the general principles underlying the structure,

behavior, and relations of organisms rather than a catalog and arrangement of their forms. But two chapters of the eighteen refer to classification at all and in these the principles of taxonomy are dwelt upon more than the results of their application. An earnest attempt is made to cover the biological field, but its great extent and the limits of the book make the treatment of many subjects necessarily brief. In some places there is apparent a lack of careful judgment of values. This shows itself, for example, in the use of some highly specialized illustrations, taken from monographs, and in certain quotations from technical papers the language of which is not entirely suited to an elementary text.

Despite these minor weaknesses, however, the book has much to commend it, especially to those looking toward a medical career. It considers modern biological problems from a real scientific standpoint and presents essential facts in their direct bearing upon everyday life. There are eighteen chapters of which the first thirteen, occupying 163 of the 285 pages, deal with general questions of morphology and physiology and the small amount of taxonomy. The remainder are devoted to more special topics under the titles "Some biological adaptations" (parasitism); "Some biological factors in disease," "Evolution." "Variation-heredity," "Animal behavior and its relation to mind." The longest chapter is the one dealing with the factors of disease and the next in length is the one concerning variation and heredity. Although the subject matter of these two chapters is widely different in some respects, the treatment of each is strictly scientific and will doubtless prove of great interest to medical men. C. A. McC.

THE SURGICAL CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. June, 1913. Pp. 185; 62 illustrations and a colored frontispiece. Philadelphia and London: W. B. Saunders Company, 1913.

THIS number of Murphy's *Clinics* contains the usual variety of interesting surgical matter, ranging from such topics as intestinal obstruction from gall-stones and procidentia uteri, to ankylosis of the jaw and fracture of the neck of the femur. An interesting clinical lecture and series of operations by Dr. Albee of New York City is included, dealing chiefly with bone transplantation in cases of Pott's disease; but Dr. Albee does not neglect the wider applications of bone transplantation to ununited fractures and congenital and acquired deformities of the limbs. The two most interesting bone cases reported by Dr. Murphy are one for arthroplasty of the hip for ankylosis the result of tuberculous disease,

and an operation for ununited fracture of the neck of the femur. The former condition, tuberculous ankylosis, is one which most surgeons, including the reviewer, have considered not suitable for arthroplasty, on account of the danger of stirring up the old disease; the motto *μὴ ζῆναι παμζῆναι* or *quieta non movere* being in no class of cases more important than in these. And it is interesting to see that Dr. Murphy after beginning the operation found an abscess close to the hip-joint, and left his patient, at last reports, with suppurating sinuses. It will be of much importance to learn the final result.

A. P. C. A.

DIET AND HYGIENE IN DISEASES OF THE SKIN. By L. DUNCAN BULKLEY, A.M., M.D., Physician to the New York Skin and Cancer Hospital; Consulting Physician to the New York Hospital. Pp. 194. New York: Paul B. Hoeber, 1913.

THERE is much to commend and recommend, also several things to criticize, in the publication of Bulkley's book on the diet and hygiene as they affect the skin. Every one should realize the importance of the generalities, emphasized in the first portion of the volume, as to the quantity, the quality, and the mode of preparation of the food, the time and the method of consumption, the nervous element, fatigue and irregular eating which may give rise to the improper digestion of the same. The value of this portion of the volume cannot be too strongly emphasized. The author relies, however, too much on urinary examinations to prove the metabolism of the individual, without ascertaining sufficiently the amount and the character of the food ingested. He considers that the greatest fault with most individuals with diseases of the skin consists in too great a quantity of nitrogen in the food. A rice diet is strongly advocated in certain cases of acute eczema and other inflammatory conditions of the skin, including erythema multiforme. A "wheat-jelly" is strongly recommended as a diet in infantile eczema. Bulkley makes the statement that a vegetarian diet is both helpful, curative, and preventive in psoriasis. Many, if not most, dermatologists will disagree with him in this statement. Most authorities will hardly agree with his belief in the effectiveness of a vegetarian regimen in mycosis fungoides, epithelioma, or alopecia.

The second portion of the volume is devoted to the hygiene of the individual and to others than the patient. The subjects mentioned are all more or less important, such as regularity of the bowels, sleep, exercise, the irritation of certain occupations, the clothing, bathing including medicated baths, and so on. Two

interesting tables are presented; the first, contains articles of food and their fuel value and the second, edible nutrients and their fuel values.

F. C. K.

DISEASES OF THE EAR. By PHILIP D. KERRISON, M.D., Professor of Otology, New York Polyclinic Medical School and Hospital, Junior Aural Surgeon to the Manhattan Eye, Ear and Throat Hospital; Aural Surgeon to the Willard Parker Hospital, etc. Pp. 588; 333 illustrations. Philadelphia: J. B. Lippincott, 1913.

IN presenting this excellent addition to the list of otological text-books the author has taken into full consideration the rapid strides otology has taken in the last few years. Emphasis is laid upon the fact that the otological surgeon has passed far beyond his former rather narrow field and has become a general intracranial surgeon.

Suppurative lesion of the brain and meninges cover nearly two hundred pages, far more space than is usually allotted to these subjects. The intricate surgery and physiology of the labyrinth are described in great detail. The chapter on serum therapy in the treatment of aural disease, embracing autogenous vaccines and the His leukocyte extract, is a distinct innovation.

In the arrangement of the subject matter the usual time honored customs have been disregarded, prominence being given to the practical side of otology and not to anatomical sequence. The illustrations are numerous, and most of them are new, being taken from original drawings by the author.

The entire work well represents the most modern otological theories, with the preservation and rearrangement of well established facts.

B. D. P.

NERVOUS AND MENTAL DISEASES. For Students and Practitioners. By CHARLES S. POTTS, M.D., Professor of Neurology in the Medico-Chirurgical College of Philadelphia, Neurologist to the Philadelphia Hospital, Formerly Associate in Neurology in the University of Pennsylvania. Third edition, revised and enlarged. Pp. 610; 141 illustrations and 6 plates. Philadelphia and New York: Lea & Febiger, 1913.

THE third edition of Dr. Potts' book on Nervous and Mental Diseases follows along the same plane of excellence noted in his former editions. The book is well printed and well illustrated,

and a good example of the bookmaker's craft. Many new features have been added, such as the importance of the Wassermann reaction, the latest view of tic, and short descriptions of some of the newer symptom-complexes, myotonia atrophica, progressive lenticular degeneration of Wilson, etc.

The chapter on symptomatology is one especially to be commended. This contains features well arranged for the student in his first study of this subject. It is unfortunate that in the chapter on hysteria, Freud's ideas are dismissed in a single paragraph.

The book approaches in some ways many of the larger works on Neurology, but misses the philosophic grasp which lends so much to the unity of such a subject. Nevertheless the work should prove valuable to the student and general practitioner, both for its conciseness and lucidity.

S. L.

SELECTED PAPERS ON HYSTERIA AND OTHER PSYCHONEUROSES.

By SIGMUND FREUD, Vienna. Authorized translation by A. A. BRILL, M.D., Ph.B., Chief of Nervous Department, Bronx Hospital and Dispensary. Second edition. Pp. 215. New York: The Journal of Nervous and Mental Disease Publishing Co.

THIS is the second edition, the only change consisting of two chapters, one on wild psycho-analysis and the other on the future chances of psycho-analytic therapy.

The mere fact that a second edition has appeared within a year of the publication of the first is an indication of the need of this work and the growth of Freud's teaching in this country. Since the appearance of the first edition many papers upon this subject have been published, and a National Society for the Study of Psycho-Analytic Method has been formed. While all this indicates that psycho-analysis is better recognized, it has not by any means minimized the spirit of antagonism which it has aroused. The reader is referred to the review of the first edition which appeared in a previous number of this JOURNAL. T. H. W.

FOR AND AGAINST EXPERIMENTS ON ANIMALS: EVIDENCE BEFORE THE ROYAL COMMISSION ON VIVISECTION. By STEPHEN PAGET, F.R.C.S., Hon. Secretary Research Defense Society. New York: Paul B. Hoeber.

THIS book should prove to be of great value to all who are interested in the important question of vivisection, which is being constantly brought before the public.

Paget, from his position as Hon. Secretary Research Defense Society has been able to obtain the evidence of both antivivisectionists and various investigators. He carefully shows the remarkable benefits which have been given to mankind during the last twenty or more years, and which were alone obtainable through experiments upon the lower animals. Innumerable instances are quoted, as the discovery by Lister of antiseptics to be followed later by asepsis, the Pasteur treatment of hydrophobia, diphtheria antitoxin, and many other prophylactic and curative methods, all of which were accomplished solely through experiments on animals, thus utterly refuting the statement which is continually being advanced by the antivivisectionists that no benefits to humanity have ever been derived by such means.

Another point advanced by those who would abolish all work upon animals, and refuted by the other side, is the excessive cruelty and suffering to which the animal is subjected. The testimony, however, before the Royal Commission, given by such men as Starling, Cushing, and Sir Victor Horsley showed that from their wide experience in the subject they had found that the greatest care is always exercised to prevent any suffering, the animals always being completely anesthetized before they are operated on, and every known method being employed to prevent post-operative discomfort, and to this evidence the opposing side was unable to prove one authentic case to the contrary.

Taken as a whole, the book gives a clear, concise, and unprejudiced statement of the findings on both sides of this very important subject, and should help once and for all to settle the question in this country, where every so often a movement is brought forward endeavoring to check all scientific research by limiting experiments on animals.

F. P., JR.

A PRACTICAL MEDICAL DICTIONARY. By THOMAS LATHROP STEDMAN, A.M., M.D., Editor of *Twentieth Century Practice of Medicine*; Editor of the *Medical Record*. Second edition. Pp. 1028. Illustrated. New York: William Wood & Company.

THE second edition of this standard dictionary from the scholarly pen of Dr. Stedman contains many admirable features. There have been incorporated in the text life insurance, dental, veterinary, botanical, electrical, homeopathic, and eclectic terms; but of particular value has been the inclusion of eponymus terms in their alphabetical order. With such terms there has been appended a short biographical sketch of the persons whose names have been applied to diseases, symptoms, signs, etc. A list of the mineral springs of America and Europe, with information as to their

chemistry and therapeutic value has also been incorporated. The pharmaceutical preparations of the United States, British, and National pharmacopœias have been added.

In the spelling Dr. Stedman has seen fit to countenance the simpler forms with consequent elimination of the diphthong æ and œ, a method of spelling which is being universally employed in this country but to which British physicians object.

The book fulfils all the demands of a medical dictionary for fulness and accuracy and can be unreservedly recommended as a thorough, exact, and careful compilation. J. H. M.

THE OCULAR MUSCLES, A PRACTICAL HANDBOOK ON THE MUSCULAR ANOMALIES OF THE EYE. By HOWARD F. HANSELL, A.M., M.D., Professor of Ophthalmology in the Jefferson Medical College; and WENDELL REBER, M.D., Professor of Ophthalmology in the Medical Department of Temple University. Second edition. Pp. 223; 3 plates and 82 illustrations. Philadelphia: P. Blakiston's Son & Co.

THE intelligent reader after mastering the contents of this book will have little to learn of the practical in the matter of the ocular muscles. There is naturally much of the theoretical which is necessarily omitted; a fuller discussion of the refraction by prisms with an elementary exposition of the mathematical theory would have been in place, but the authors have laid emphasis more especially upon the needs of those for whom the book seems intended. The practitioner who is interested in the anomalies of the ocular muscles will find this handbook a clear and reliable guide to which he can confidently turn.

It is particularly satisfactory to note the sane views the writers take on the subject of heterophoria. A half-dozen purely ocular symptoms are clearly stated. Of the reflex symptoms, headaches—with nausea, vomiting, and vertigo—are very properly connected with heterophoria, but no extravagant claims are made. As regards epilepsy, we quote: "We believe it is the latter class of cases (vertigo with momentary unconsciousness, etc.) that are vaunted by many as instances of essential epilepsy partially or even entirely curable by eye-treatment alone."

Operative treatment is recommended as a last resort in esophoria; in exorophoria, the choice is between tenotomy and advancement when other measures have failed. While in hyperphoria, operation is narrowed down to where the deviation tendency is constant and when all tests agree in showing marked over- or under-action of one set of elevators or depressors, the use of prisms and exercise having been without avail. T. B. S.

DIE CHIURGISCHEN UNTERSUCHUNGS-METHODEN. By PROFESSOR DR. HUBERT GEBBELE. Pp. 184; 154 illustrations. Munich: J. F. Lehmanns.

GEBBELE has condensed the essentials of surgical diagnosis into a small volume. After a page and a half devoted to the importance of the history and the method of taking it, he considers the various physical signs elicited by inspection, palpation, percussion and auscultation. The passage of sounds into the esophagus and stomach, the rectum, and the urethra, and the diagnostic indications for the hollow needle and exploratory incision, are discussed. Other chapters are given to the methods of examining the secretions and excretions, and the blood. Serodiagnostics, endoscopy, and radiography are also dealt with. The author aims at stimulating independent, systematic investigation and does not enumerate in detail the symptoms of the conditions described and illustrated. The book serves well the purpose for which it was written, and will be useful not only to the young but the older physicians as well.

T. T. T.

A PRACTICAL TEXT-BOOK OF THE DISEASES OF WOMEN. By ARTHUR H. N. LEWERS, M.D., Senior Obstetric Physician to the London Hospital. Seventh edition; pp. 530. New York: Paul B. Hoeber, 1912.

THIS work doubtless serves as a text-book to the students taught by the author, and as such will fulfill its purpose admirably. It is, however, too markedly an expression of the personal opinions of the author, to the exclusion of other and well tried methods of treatment, ever to be of great value to students other than his own. The first chapter is excellent and contains a detailed description of the methods of taking the history and examination of a patient, which could well be imitated by other text-books on this and similar subjects. It is regrettable that as much cannot be said for the remainder of the book. Here, when we have long ago given up such methods as archaic, it seems strange to find recommendations to dilate the cervix by Higar's bougies and by tents; to recommend the Tait operation as the only method of perineorrhaphy; to find no mention of the Schatz metranoikter in the treatment of dysmenorrhea and sterility, to mention only a few of the more obvious points. The book is based upon a small experience (1083 abdominal sections in eleven years; 2 a week), and will hardly appeal strongly to the profession in this country.

J. C. H.

THE TREATMENT OF SHORT SIGHT. AN ELABORATION OF THE LECTURE GIVEN EACH YEAR TO HIS STUDENTS. By PROFESSOR HIRSCHBERG. Translated into English by G. L. JOHNSON. Pp. 123; 10 illustrations. New York: Rebman Co.

ANY discussion upon this subject by one who has had the opportunity to observe this condition in a large number of patients is, of course, worthy of thoughtful consideration. Professor Hirschberg, by reason of his residence in Germany, where myopia is so unusually prevalent, and because of his many years of practice, has thoroughly studied this condition. Being an observer of unusual acuteness, his presentation of this subject has resulted in a real and valuable contribution to ophthalmic literature.

So vivid is his portrayal of myopia as it progresses through the consecutive stages of the pernicious form, that the reader can, in a short space of time, have a grasp of the subject that would perhaps take years of observation of an individual case to duplicate.

The reader will be impressed with the sincerity of the author's convictions, and will find a second reading of this unique book time well expended.

B. F. B., JR.

STUDIES IN CANCER AND ALLIED SUBJECTS. PATHOLOGY. Conducted under the George Crocker Special Research Fund at Columbia University. Volume II; pp. 267; 32 plates and numerous charts. New York: Columbia University Press.

THIS report is made up of a series of twenty-seven articles, all of which have been published independently. The workers who have furnished most of the material are Isaac Levin, and Robert A. Lambert, the former having as his associate in several articles; M. J. Sittenfeld, Lambert being assisted by Frederick M. Hanes. Robert T. Frank has contributed two articles, in one of which he was assisted by A. Unger. The studies deal with a wide variety of the phases of cancer study, including a consideration of ethnological relations, heredity, etiology, immunity, metastasis formation, biological chemistry, and tissue cultivation. Nearly all the studies are experimental in nature, and present a careful analysis and consideration of the new facts learned.

A valuable feature of the work is W. G. MacCallum's introduction, which briefly summarizes, in an admirable fashion, our modern views as to the etiology, biology, and therapy of cancer.

H. T. K.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Research on Pellagra.—G. VOLTINO (*Pathologica*, 1913, v, 174) finds that the intramuscular injection into pellagrins of the aqueous extract of spoiled maize causes fever, nervous and psychic symptoms, vomiting, diarrhea, and tachycardia. The similar injection of extracts of good maize causes none of these symptoms. The active principle of the potent extract is carried down by an alcoholic precipitate, and is active in doses of 1 c.c. of a 0.5 per cent. solution. Such inoculations cause reactions in 90 per cent. of pellagrous subjects, and in about 20 per cent. of the non-pellagrous; the reaction in the latter group, he thinks may be due to eating of maize or other cereals, or it may be an evidence of "latent pellagra." Voltino designates the reagent "pellagrogenina;" it is non-toxic to rabbits fed in the usual manner, but to maize-fed rabbits, 1 c.c. of a 1 per cent. solution is fatal within twenty-four hours. The injections were made intraperitoneally. He also finds that guinea-pigs fed mainly on maize die after being injected with 1 c.c. of the serum of a pellagrin, whereas normally fed pigs are in no way affected. Maize-fed guinea-pigs treated several times with pellagrogenina readily survive the subsequent injection of serum from pellagrous patients. No microorganisms could be demonstrated microscopically or by cultural methods.

Lipoid Chemistry of the Blood—The discovery that cholesterin may occur in the blood in a free form is not unimportant, in view of the known neutralizing action it exerts upon saponin and cobra venom hemolysis. It may well be that it has a similar effect in the body upon the toxins of various acute infections. Rohmann believes that a relative increase of the free over the bound cholesterin is characteristic

of sera giving a positive Wassermann reaction, while Peritz claims to have found a constant increase of lecithin in the sera of tabetics, and ascribes to this the positive reactions. BÜRGER AND BEUMER (*Berl. klin. Woch.*, 1913, 1, 112) have investigated the sera of 21 individuals suffering from a variety of conditions. Serum was dried at 40° C. and extracted for two days with alcohol and chloroform; after weighing, the extracts were redissolved in ether and reprecipitated with acetone. The filtrate was divided into two portions; in one the cholesterin was thrown down with digitonin according to the method of Windaus, while in the other this was effected by saponification with freshly prepared sodium alcoholate. The difference between the two determinations gave the cholesterin made free from esters. Lecithin and phosphoric acid were also estimated. The highest cholesterin values were obtained in cases of diabetes, cholemia, and eclampsia, the lowest in cases of pernicious anemia, chlorosis, and inanition. In general, lecithin runs parallel with cholesterin; free cholesterin tends not to fall lower than 30 per cent. of the total cholesterin content of the blood. Bürger and Beumer were unable to confirm Rohmann's contention; in many cases the Wassermann was negative in sera unusually rich in lecithin, while in 2 cases of tabes and 1 of tertiary lues showing pronounced reactions, there were no cholesterin values obtained and lecithin was decreased. While believing that there is a definite relation between a positive Wassermann reaction and lipoids in the blood, Bürger and Beumer contend that this consists of something more than a mere increase in the two components under discussion. The exact significance of the numerous lipoids will continue to be a matter of speculation so long as we remain in ignorance of their genesis.

Quantitative Estimation of Urates in the Blood.—According to ZIEGLER (*Münch. med. Woch.*, 1913, lx, 1083) there have been two sources of error which may be held accountable for the failure of methods hitherto used to estimate the content of the blood serum in urates: (1) No method of protein removal gets rid of all the nitrogen; the so-called "rest nitrogen" results in uric acid determinations constantly higher than they should be; (2) deproteidization, moreover, removes a not inconsiderable portion of the uric acid present; (3) all methods have required relatively large amounts of blood and considerable time. To meet these defects Ziegler endeavored to discover a way of throwing down the uric acid while leaving the proteins in solution. The method is based upon the fact that copper sulphate forms a compound with uric acid, urates, and purins in general, which is insoluble in water; experiments showed that this compound remains quantitatively insoluble in the presence of a known concentration of NaOH. To perform the test, the following solutions are necessary: (1) NaOH, 4 per cent. solution; (2) NaHCO₃, 5 per cent. solution; (3) Neutral sodium sulphate, 3.5 per cent. solution; (4) CuSO₄, 2.5 per cent. solution; (5) A standardized solution of K₂MnO₄. Into a 200 c.c. Ehrlenmeyer flask containing 10 c.c. of clear serum, one adds 10 c.c. of solution 1, 20 c.c. of solution 2, and 10 c.c. of solution 3, and 20 c.c. of distilled water, in the order given. To the resulting mixture, one adds, while shaking, 10 c.c. of solution

4, from a pipette; a clear blue-violet solution results. Pour into an evaporating dish and boil until about one-third of the original volume has gone, at which time a gray-white precipitate comes down. Pour into a centrifuge tube, washing the evaporating dish well, and centrifuge at high speed, draw off the clear blue superwatered fluid, mix the precipitate well with water, centrifuge, and repeat until the fluid remains absolutely clear, colorless, and incapable of producing foam when shaken, this being a trustworthy test for the absence of protein. The sediment, now colloid free, is dissolved in 10 c.c. of concentrated H_2SO_4 , and the uric acid determined by titrating with a solution of K_2MnO_4 . It may be best to add a known amount of uric acid and, say, 0.01 gram, and titrate the difference. The serum used must be fresh, preferably sterile, and absolutely free from blood. The method will detect 0.005 to 0.025 gram of uric acid per 10 c.c. of serum, is relatively simple, and requires only an hour's time.

Addison's Disease.—Lowy (*Deutsch. Archiv f. klin. Med.*, 1913, cx, 373) presents a case of Addison's disease, diagnosticated clinically by reason of the marked pigmentation, myasthenia, diarrhea, emaciation, hypothermia, and low blood pressure, these symptoms occurring in association with rapid mental deterioration in a man, aged twenty-one years, who had previously been of more than average intelligence. Tuberculin tests were negative; there was no marked anemia, but a lymphocytosis of 33 per cent., and a mild grade of eosinophilia. At autopsy the interesting findings were, first the complete absence of the specific cellular elements of the cortex of both adrenals, which were composed entirely of medullary parenchyma and second the existence of a well-developed status thymicolymphaticus. Hedinger had previously called attention to the fact that in 15 cases of Addison's disease 7 showed the existence of a status thymicolymphaticus, while in 5 others there was pronounced lymphatic hyperplasia, and he expressed the idea first advanced by Wiesel that in these cases the normal balance between the lymphatic glands and chromaffin system had been disturbed through deficiency in the latter, to which was to be ascribed both the glandular hyperplasia and the various manifestations of Addison's disease. This theory was opposed to that which assumes that the cause of Addison's disease is to be found in the cortex of the adrenals; it has, moreover, been shown experimentally in animals that the adrenal cortex is necessary for life, a finding apparently confirmed in this case. The persistently low blood pressure, despite the apparent integrity of the adrenalin-producing cells, leads to the conjecture as to whether or not the thymus may have been responsible, Mohr having shown that thymus extracts are capable of producing tachycardia, asthenia, and low vascular tonus. Moreover, the embryological relationship between the "interrenal" system and the brain may in some way be turned to account for the pronounced mental changes observed in this case. Clinically the frequency with which Addison's disease is accompanied by a status lymphaticus should make one very careful to avoid any procedure apt to induce psychic disturbances, and a sudden lethal result. The relatively characteristic blood picture of Addison's disease finds reasonable explanation in the coincident glandular hypertrophy and recently

Weidenreich has shown that the thymus itself may be a source not only of lymphoid elements, but also of the granular cells and eosinophiles in particular.

The Irritative Effects of Ascaris on the Intestines of Man.—J. C. HUBER (*Münch. med. Woch.*, 1912, lix, 2669) reports a noteworthy case of ascaris infection. The patient, a boy, aged thirteen years, had suffered for two years from periodic attacks of pain in the right iliac fossa. Every two weeks or so, ascarides were passed with the stools. Huber saw the patient suffering with sharp pains in the right iliac fossa and vomiting. His temperature was 37.6, pulse 90. There was tenderness at McBurney's point and diminished resonance in the right iliac fossa. No mass was palpable. Appendicitis was diagnosed and laparotomy performed. A moderate amount (50 to 510 c.c.) of free serous fluid was found on opening the abdomen. The appendix was perfectly normal in appearance. The ileum, however, for a distance of about 20 cm. showed a reddened serosa and plainly dilated lymph channels in the subserous layers. This extended to within 8 to 10 cm. of the ileocecal valve. In the mesentery of the congested part of the gut moderate swelling of the glands was visible and palpable. In the congested part and just above it one could feel worm-like bodies, evidently ascarides. Four days after the operation, seventeen ascarides were passed spontaneously. After administering santonin and calomel, forth-nine more worms were obtained. Huber suspects that such attacks as his patient suffered from are not rare in ascaris infections, though the lesions may not always be so evident. The possibility should be considered, especially in patients known to be infected with *Ascaris lumbricoides*.

Superpermeability in Nephritis.—BAETJER, during the study of renal function in the various clinical types of nephritis (*Arch. Int. Med.*, 1913, xi, 593) was impressed with a certain peculiarity common to 4 cases, namely a supranormal excretion of some of the substances employed. All were outspoken clinical cases of chronic nephritis with edema and large content of albumin in the urine. In 3 of them the phthalein elimination was well above normal, 83 to 90 per cent., for two hours. The lactose test showed the same tendency—in one and two hours, in 2 of the cases, a marked increase in rapidity of excretion. In 2 cases there was a definite delay in the elimination of potassium iodide, sixty-eight and seventy-two hours. But in common to all was the impaired salt elimination, the one test which gave evidence of functional renal impairment in these cases. The association was of an impaired sodium chloride elimination with a supranormal excretion of lactose and phthalein. Baetjer believes that there may exist in some types of nephritis a stage in which the kidney is hyperpermeable, at least to some substances used for functional tests, with an elective impermeability for chlorides. This fact emphasizes the need of studying renal function from the standpoint of a considerable series of functional tests rather than to draw conclusions from the excretion of any one drug. Similar observations, as Baetjer points out, have been made as to the elimination of other coloring matters, notably by Bard, Bernard, and Castaigne, in connection with methylene blue.

SURGERY

UNDER THE CHARGE OF

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Operation upon Paralytic Feet.—MÜLLER (*Zentralbl. f. Chir.*, 1913, xl, 312) presents an operation for paralytic talipes calcaneus, which is indicated in those cases in which the gastrocnemius and soleus are paralyzed and the other muscles on the posterior side of the leg are preserved. As a substitute for the calf muscles, he takes on the inner side the flexor longus hallucis and on the outer side the peroneus brevis. A longitudinal incision, extending from one side of the limb to the other, is made between the tibia and fibula in front and the tendo-Achilles behind, and extending to the junction of the lateral surface of the tuberosity of the calcaneum and the posterior surface. Above, the incision is deepened to the flexor longus hallucis and peroneus brevis and below to the bony surface of the calcaneum. The latter is denuded of its fibroperiosteal covering and two small holes are drilled transversely through the tuberosity, one close above the other, and both very close to the posterior surface of the bone. Another incision is made along the external border of the foot to expose the tendon of the peroneus brevis which is then separated from its insertion to the fifth metatarsal bone. A fourth incision along the inner border of the foot exposes the tendon of the extensor longus hallucis, so that it can be divided in the middle of the sole of the foot. It is easily followed by passing a grooved director along its sheath from the inner side of the first double or through-and-through incision. The ends of the two divided tendons are brought, one out of each side of the first incision, and each is passed through one of the transverse canals in the tuberosity of the os calcis, so that the tendon of the flexor longus hallucis passes into the mouth of one canal and out of its external opening, and that of the peroneus brevis in the reverse direction through the other bony canal. The end of each tendon is then clamped with a forceps, and while the foot is strongly flexed in the plantar direction, the ends of the tendons are bound together. The two muscles then form a two-headed muscle inserted into the tuberosity of the os calcis. The tendo-Achilles is now shortened so that it will help mechanically to hold up the heel. The foot is kept in strong plantar flexion for four or five weeks, in a plaster cast. After the cast is removed, the foot is gradually brought to a right-angle position by exercises. Gradually plantar flexion is acquired,

so that in walking the anterior part of the foot is on the ground and the heel is raised. While not normal, walking becomes not much removed from normal. Müller objects to the usual arthrodesis of the ankle-joint in paralysis of the muscles of the foot and prefers arthrodesis of the astragalotarsal joint. The posterior part of the foot, by this operation, acquires firmness because the astragalus, calcaneus, scaphoid, and cuboid are bound together in one bony mass. The necessary flexion and extension of the ankle-joint are preserved, while all lateral movements are excluded.

Experimental Ligation of the Portal Vein; Its Application to the Treatment of Suppurative Pylephlebitis.—NEUHOFF (*Surg., Gynec., and Obstet.*, 1913, xvi, 481) says that the fact that no surgery of the portal vein has as yet developed appears to depend upon the results of animal experimental studies. He made an experimental study, comparing his results with those of other workers, and concludes that experimental complete ligation of the portal vein is immediately fatal. Death results from shock. Apparently normal life is compatible with complete occlusion of the portal vein, if gradually induced. This is true for the human being and the experiment. In the latter, gradual obliteration of the lumen can be successfully induced in a very brief period. The liver remains practically normal with complete occlusion of the portal vein existing for a short time (experimentally), and for very prolonged periods (clinically). The reason for this lies chiefly in the development of a hepatoportal circulation. The latter is demonstrable clinically and experimentally. In the experiment the hepatoportal circulation appears to develop regularly in the gastro-hepatic omentum. An active treatment of suppurative pyelephlebitis is suggested on the basis of his summarized results. Ligation of the portal vein, with the modifications embodied in the paper, is the treatment that is advocated. The operation is worthy of a trial in an attempt to improve the results of an affection so regularly fatal.

Studies Concerning the Comparative Value of Non-pedunculated Flaps of Omentum, Peritoneum, and Mesentery, for the Reinforcement of Sutures.—SASAKI (*Deut. Zschr. f. Chir.*, 1913, cxiii, 62) says that peritoneal or mesenteric flaps are of substantial value for suture insufficiency in all abdominal operations. Omental flaps, on the other hand, are not deserving of much attention. The first two can take the place of the Lembert seromuscular suture, the last cannot. The striking difference in the results of the employment of these three kinds of flaps, depends chiefly upon the presence or absence in the flaps of the network of elastic tissue. The chief effect of this elastic tissue lies in the fact that with it the flaps can adapt themselves closely to the underlying layer and in the fact that the specific elasticity presents an unbroken resistance to the internal pressure of the gastrointestinal tube. The healing process can then go on favorably. Omental flaps do not favor these results because of the irregularity of its structure, its abundance of fat, the difficulty with which it applies itself, and its greater mass. Unfavorable conditions accompanied their employment, as contraction or adhesion of the flaps, with often produced restriction of the passage of the intestinal contents. The essentials

for healing, whether it concerns a double or single row of sutures, consists in the adhesion and growth of the apposed serous surfaces and the inner surface of the flap applied to the intestinal serosa, which with time organizes and is finally changed into cicatricial tissue. The healing, while completed by the regeneration process, is reinforced by the covering of the defect by endothelium. This endothelial covering is, unconditionally, dependent upon the vitality of the flap. Therefore, autoplasty gives the best results. Homoioplastic peritoneal flaps may also succeed unless necrosis occurs. Their permanent preservation, however, is very questionable. They appear to live until the defect is covered by mucous membrane. The use of a hernial sac from another individual may prove practical. When perforation of the omental flap was observed it occurred as a rule in the middle of the applied flap. The kind of suture, whether interrupted or continuous, had no influence on the perforation. One may often leave a peritoneal defect, because the endothelium can cover it from the surrounding part, after some time. In order to prevent adhesions, the defect may be closed by sutures. The flap may be employed as a prophylactic measure, when the stomach or intestinal suture cannot be relied on, when there is strong tension on the suture or the serosa is defective, and in any circumstances where such postoperative danger exists. It is also useful when there is a loss of substance after separation of adhesions, and with reserve it may be recommended in gastric and duodenal ulcers.

Function Tests in Connection with Transplanted Kidneys.—LOBENHOFFER (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxvi, 197) says that many experimental studies have been made from the anatomical as well as the physiological standpoints, to clear up the many questions concerned with the innervation of the kidneys. The purpose of his investigations was to study the manifestations of life of the transplanted kidneys in relation to our present knowledge. That such a kidney could supply the body with its normal function was known, but whether it could meet increased demands had not been studied. One may be deterred from undertaking further experiments on an animal on which a successful transplanation and nephrectomy have been done, because of the fear of killing it. The histological examination showed that the successfully transplanted kidney possessed, in a normal manner, the most delicate and sensitive structures in which lay the power of function. When the secreting cells lost their activity, the granules disappeared before anything else. For a permanent normal secretion the proper proportion of the normal constituents must be preserved and for this the nervous influence is necessary. The experiments sought to test the functional capacity of the tubular and vascular portions of the kidney. The investigations show that there was no considerable deviation from the normal in the activity of the transplanted kidney. The elimination of water and saline solution and the effect of foreign substances like milk sugar and phloridzin were tested. Since the experiments were carried out only on healthy animals which lived a long time in complete health, the conclusion is justified that the other functions of the kidney are performed in a proper manner. One may conclude that the successfully transplanted kidney

will meet not only all normal demands but those greater than normal. The normal urine secreted during diuresis caused by hydremia gives perfect proof that the vascular system of the transplanted kidney is complete. The work of the vessels is dependent upon the contractile elements and this again can only be due to the nervous influence. Since every nerve impulse to the transplanted kidney is cut off, the intrarenal plexus must be so far independent that it alone must exercise every necessary automatic impulse for the work of the kidney. This seems indisputable and is to be explained by the physiology. It shows that the nerve branches entering at the hilum give no specific secretory branches to the epithelium, since in a transplanted kidney the epithelial function could not be normal. At the present time, however, it would not be justifiable to conclude that the secretory filaments must come from the intrarenal plexus. Our knowledge of the nerve influence upon secretion is not yet definite enough to permit one to drawing binding conclusions. The Eckhard theory of the existence of a secretory centre for the kidney in the spinal cord cannot be wholly right. The branches to the kidney from the spinal cord and sympathetic must play a subordinate part. They probably interpose a regulating influence. There are probably other branches upon which the task falls to convey impulses centripetally and to cause reflex effects in other organs.

Concerning Immunity against Pancreatic Necrosis.—JOSEPH and PRINGSHEIM (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1913, xxvi, 290) say that the experimental work that has been done during the past ten years on pancreatic and fat necrosis has been concerned chiefly with two points. In the first place the workers have attempted to produce in animals characteristic pancreatic and fat necrosis, with the object of obtaining light on the origin of the local affection. In the second place the efforts have been directed toward learning the cause of the severe, mostly fatal, general symptoms and thus drawing nearer to an effective method of combating them. They conducted a series of experiments with these ends in view and believe that they have contributed as much to the solution of the pathogenesis as have the recent investigations of Fischler. Fischler found that an animal with an Eck fistula (between the portal vein and inferior cava) showed after death all kinds of degeneration of the liver parenchyma in severe grade, and frequently died with severe symptoms of auto-intoxication. In these foci of degeneration he demonstrated the products of fat splitting by steapsin and brought them into relation with mild pancreatic lesions from operation and fat necrosis. In this way a causal relationship was constructed between pancreatic necrosis, loss of function of the liver from an Eck fistula, and fatal antointoxication. As Guleke and von Bergmann had already shown, a preliminary subcutaneous treatment of dogs with trypsin, provides protection not only against the toxic effect of larger doses of trypsin, but also against the toxic effect of pancreatic substance introduced into the peritoneal cavity. Their experiments show that the immunity is provided only against a certain amount of the pancreatic substance in the peritoneal cavity. In order to provide further protection, the embedding of the pancreatic substance into the peritoneal cavity must be preceded

by an immunization with increasing doses. These experiments furnish a further support for the view that the toxic effect of the necrotic pancreas does not depend alone upon the toxic effects of its proteolytic ferment. The immunity obtained by preliminary treatment with trypsin and pancreatic substance cannot be transferred to other animals.

THERAPEUTICS

UNDER THE CHARGE OF

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The Interpretation of the Results of the Wassermann Test.—CRAIG (*Jour. Amer. Med. Assoc.*, 1913, lx, 565) gives his interpretation of the results of the Wassermann test after antiluetic treatment. The conclusions regarding the interpretation of the Wassermann test were derived from the study of 10,000 tests made in the Army Laboratory in Washington. The total number of individuals tested has been 5216, while 4784 reëxaminations were made generally as a control of the treatment. In the vast majority of the 4784 reëxaminations the test was made for the purpose of controlling treatment with salvarsan, mercurials, or both. The results have demonstrated the great value of the Wassermann reaction as an index of the efficiency of treatment and it has been possible to trace the gradual disappearance of the reaction in treated cases and its reappearance in those instances in which further treatment was required. The use of the reaction in this manner has made possible the intelligent administration of both salvarsan and mercury and every patient suffering from syphilis should have the treatment controlled by Wassermann tests made at intervals of at least two months. Only in this way can justice be done the patient and the specific treatment of syphilis be conducted in an adequate and scientific manner. The occurrence of a double-plus or plus reaction following treatment should always be interpreted as meaning that more treatment is necessary. Granted that as most observers believe, the presence of a positive Wassermann reaction means the presence of living spirochetes, it is evident that when such a result is obtained the patient cannot be considered as cured, even though symptoms may have been absent for months or even years. A plus-minus reaction after treatment, provided it is obtained on repeated examinations, should also be considered as an indication for more treatment, but when such a reaction is obtained treatment should not be given until the test has been repeated, unless symptoms are present. A negative reaction after treatment is of no value as an evidence of cure unless it remains negative for at least a year and no symptoms have developed meanwhile. The limit of a year is arbitrary and founded on the experience in controlling the treatment in hundreds

of cases of syphilis. Only one relapse was observed, in a patient whose Wassermann reaction has remained negative for a year after the cessation of treatment. A luetin test should also be made, even though the Wassermann test is negative.

Fatal Result Following Benzol Treatment of Leukemia.—JESPERSEN (*Deutsch. med. Woch.*, 1913, xxxix, 1300) reports a case of myeloid leukemia treated by benzol in which the improvement at first was very marked. In the course of the first ten days of benzol treatment the leukocyte count fell from 250,000 to 61,000. This fall in the leukocytes was accompanied by a considerable improvement in the general condition without, however, an appreciable effect on the side of the liver or spleen. On the seventeenth day of treatment the red blood count had increased from 2,000,000 to 3,250,000, but on the following day a severe epistaxis occurred and the benzol was discontinued. The condition of the patient became very grave, the red blood cells falling below 2,000,000. After a benzol free period of twelve days benzol was again given in larger doses, up to 5 gm. a day, giving during the following thirty-two days a total amount of 97 gm. of the drug. There were no untoward symptoms and no evidence on the part of the urine of any toxic action. During this period marked improvement in the general condition occurred and the leukocyte count fell to 5,000 per c.c. The spleen and liver decreased markedly in size and the patient was cured so far as subjective symptoms were concerned. In a later note to the article Jespersen relates a rapid recurrence of all the symptoms. Ten days after the count of 5,000 the leukocytes had risen to 300,000, the liver and spleen rapidly enlarged, the fever returned, severe epistaxis and uncontrollable vomiting developed and the patient died twenty-three days after the apparent cure. During this recurrence benzol was again given systematically, except during the last ten days when the vomiting did not permit of the remedy. The blood count on the last day showed a rise of leukocytes to 750,000 and the reds showed changes resembling those of pernicious anemia. Jespersen does not believe that these symptoms were due to benzol poisoning but that they were due to a recurrence of the leukemia in a more acute form.

Diuretics in Cardiac Disease.—HIRSCHFELDER (*Jour. Amer. Med. Assoc.*, 1913, lxi, 340) says that in considering the subject of diuretics in cardiac disease it is essential to have some tentative idea of the forms of cardiac disease in which it is desirable to resort to diuretics to all; secondly, that we form a clear idea of the manner in which the lesion of the heart effects the action of the kidney; and thirdly, that we consider the mode of action by virtue of which the particular diuretic drugs under consideration may be expected to remedy these disturbed conditions. Hirschfelder mentions five forms of disease of the circulation in which resorting to diuretic measures might be advisable: (1) infective endocarditis; (2) arteriosclerosis with periodic attacks of the various disturbances associated with localized arteriosclerosis, vertigo, headaches, transitory cardiac asthma or pulmonary edema, angina pectoris, and vasomotor crises; (3) chronic or paroxysmal hypertension without edema; (4) acute cardiac overstrain, and (5)

broken systemic compensation with chronic passive congestion and edema with or without general anasarca, ascites, hydrothorax, or hydropericardium, arising from myocardial weakness, valvular insufficiency, or adherent pericardium. Acute and chronic infective endocarditis is associated with a scanty urine with albumin and red blood cells, but this is due to the presence of a true infective glomerulonephritis, and should accordingly be treated as a primary nephritis rather than as a primary heart disease. In the group of arteriosclerosis and of chronic hypertension as von Noorden has shown, it is better to spare the arteries and kidneys from overwork by light diet and restriction of salt and water than to remove these substances from the system with diuretics. In acute cardiac overstrain, the diminution of urine is of transitory duration and clears up when the strain is removed. The chief condition in which active intervention to induce diuresis is advisable is in the group of cases of broken compensation with chronic passive congestion. The functional power of the kidney in passive congestion is extremely variable and may be easily determined by the different functional tests. It is possible to determine by these tests if the tubules or the glomeruli are chiefly at fault and to select the remedies most suitable. The diuretic action of digitalis depends on its action in the circulation, the velocity of blood flow, and the pulse pressure. If the diminished urine output is due to failure of the filtration through the glomeruli it is possible to increase filtration through glomeruli by digitalis preparations. This action is marked in cases of cardiac irregularity and especially in patients with auricular fibrillation. In using digitalis it is important to obtain a preparation which has been standardized physiologically in order to secure sufficient dosage, but aside from this Hirschfelder does not think there is any essential differing in the choice of the preparation to be used. Digitalis infusion probably contains more digitoxin than the other preparations, but he does not think a good infusion is more efficacious than an equally good tincture, whereas, on the other hand, infusions are more subject to variation and spoiling. Strophanthin in doses of from 0.5 to 1 mg. injected intravenously or intramuscularly is also an excellent diuretic. Other members of the digitalis group—squill, convallaria, adonis vernalis, hellebore, etc., are in general inferior to digitalis. Where a more powerful diuretic action is desired than is afforded by digitalis, the diuretics of the purin group are indicated, such as caffein, theobromin, theophyllin or theocin which act by dilating the renal vessels and by direct action on the epithelium. Of this group the most convenient form of all is the water-soluble acet-theocin sodium in doses of about three grains three times a day; it not only gives greater diuresis, but may also cause diuresis in cases in which theobromin sodium salicylate evoked no response whatever. Members of this group should be used with caution since they may actually diminish renal secretion when the kidney cells are much damaged. It is necessary to make a preliminary phthalein test to determine in any given case the exact extent to which the renal epithelium is injured. If the phthalein excretion is low—30 per cent. or less in two hours—we know at once that we are somewhere near the point at which theocin might injure the renal epithelium; and it will be better to rely on the digitalis and try to improve the circulation before trying to stimulate the kidney.

If the general circulation improves, the function of the renal epithelium will return very rapidly to nearly normal, and then one need not be afraid of acting on it with these powerful diuretics. Therefore, we should aim first to improve the circulation with digitalis and leave the removal of the edema for the administration of caffein diuretics. The good effects of calomel in cardiac disease is testified to by its long empirical use. Calomel acts particularly on the tubules, and tends to increase the excretion of sodium chloride more than the total volume of urine. However, it must not be forgotten that calomel acts on the kidney by being converted to mercuric chloride and that any excess may give rise to a bichloride nephritis which affects chiefly the tubules. It is particularly dangerous, therefore, in cases in which the renal epithelium is already badly damaged, and the precaution of a phthalein test is therefore doubly advisable. There are many purely physical measures that affect the excreting power of the kidney such as removal of ascitic fluid by paracentesis, tapping a hydrothorax or a venesection. After venesection, the circulation through the kidney is probably accelerated by a decrease of blood viscosity. Hot packs or poultices over the kidneys and intestinal irrigations may also cause further dilatation of the kidney vessels from heat alone, and thus brings on diuresis. Rest to the kidney is secured by dietetic measures, such as the Karell diet, limitation of water intake, limiting the ingestion of salt, etc. In general Hirschfelder says one should aim first to know the exact state of the kidneys; second, to improve the circulation with digitalis and to spare it with the Karell diet, and thirdly to resort to theocin or the saline diuretics to relieve edema if the renal epithelium is not severely injured.

PEDIATRICS

UNDER THE CHARGE OF

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Cyclic Vomiting in Children.—HUGH T. ASHBY (*Practitioner*, 1913, xci, 53) gives this following description of cyclic vomiting. The chief feature is incessant vomiting lasting from twelve hours to several days. The attacks come on without any warning during a period of good health. Children subject to them are nearly always of a neurotic stock. The diagnosis is often difficult where no history of a previous attack can be obtained. Other signs of disease are usually lacking. The absence of much rise in temperature, quick pulse, sweetish smell of the breath, and the presence of acetone and diacetic acid in the urine will aid in forming a definite diagnosis. As many other diseases of childhood begin with vomiting these must be excluded. If the vomiting continues more than twenty-four hours without any other signs appearing it is usually cyclic vomiting. The prognosis is generally

good although the condition is accompanied by much exhaustion and a run down condition. The condition seems to be allied to delayed chloroform poisoning, although the results are not so fatal. The attacks may begin soon after the twelfth month. They tend to become less frequent and severe and usually die out by the time of puberty. Intervals between the attacks vary from three or four weeks to once or twice a year. The chief pathological feature determined is the presence during the attacks of an acidosis, or acetone and diacetic acid in the urine and breath. The most plausible theory is that there is an intestinal toxemia due to disturbance of the liver function causing the presence of acetone and diacetic acid. Postmortem findings show fatty degeneration in most of the internal organs similar to that of chloroform poisoning. Mellanby found creatin excreted in the urine only under such conditions, the amount increasing as the attack came on. On the theory that the carbohydrates are absent or not utilizable in this condition the treatment is to give large quantities of sugar by mouth during the attacks, in the form of glucose and soda-water. Glucose is also given by rectum in large quantities. The intestine is kept free by enemas. This treatment gives better results than sodium bicarbonate in large doses.

The Diagnosis of Tuberculous, Bronchial, and Mediastinal Glands.—J. H. ELLIOTT (*Canadian Med. Assoc. Jour.*, 1913, iii, 679) says that practically all children with tuberculosis have involvement of these glands. In European cities over half of the children from the fourth to the eleventh year are tuberculous. In 920 children dead from all causes in Paris, 538 showed gross tuberculous lesions at autopsy. All stages of tuberculous disease affect the bronchial glands just as they do the cervical glands.

The constitutional symptoms are those long known under the name scrofula. Pressure symptoms may include those following pressure on the trachea or bronchus, the aorta and bloodvessels of the mediastinum, or the pneumogastric and other nerves. Rupture of a caseating gland may occur into a bronchus, the trachea, the lung, or into a bloodvessel. Toxic symptoms show malaise, anorexia, anemia, and loss of weight. Pressure symptoms include cough, dyspnea, asthma, and bronchitis. Physical signs include unilateral dilated veins, slight puffiness of the face and eyelids, unequal expansion of the apices, and unilateral or bilateral flattening or retraction. Tenderness over the upper thoracic spines, especially the fifth, and tenderness over the manubrium is suggestive. Dulness on percussion over the intercostal spaces, especially the first and second on the right side is valuable, denoting enlargement of the anterior mediastinal group. Dulness on percussion below the fourth thoracic vertebra is not normal and suggests mediastinal tumor. There may be interscapular dulness from the second to the fifth dorsal spines. Bronchial breathing and bronchophonic voice sounds may be found over these areas of paravertebral dulness. The x-rays are extremely valuable in diagnosis as they show up appreciable enlargement of glands and the degree of invasion of the lungs. Of the tuberculin tests the Von Pirquet is the most useful. However, a negative reaction does not exclude tuberculosis. Elliot thinks it may be absent in some quiescent closed cases, in some advanced active cases, and in so-called refractory cases.

Appendicitis in Children.—G. C. E. SIMPSON (*Brit. Jour. Child. Dis.*, 1913, x, 400) reports his conclusions on 34 cases of appendicitis in children. The general impression is that these cases are increasing of late years both in number and severity, and hospital records apparently bear this out. In 30 cases of Simpson's, fecal concretions were found in 18. The concretions appeared to determine the site of ulceration and gangrene. The cases in general showed a tendency to early perforation and gangrene; among the 30 cases only 3 showed the mischief still confined to the appendix at time of operation. General peritonitis was present in 13 cases and in 9 others there was spreading peritonitis. Of 12 cases under eight years all had perforated. Out of the 30 cases only six admitted of primary closure. Five cases died. Earlier recognition of the symptoms and earlier operation will prevent many of the deaths. In this series severe abdominal pain was an early symptom in all save one. Vomiting occurred in 25 cases, constipation was a prominent feature in 10 cases; pyrexia was absent on admission in only 2 cases. Marked tenderness and rigidity over the right iliac fossa were present in 28 cases. Diminished mobility of some part of the abdomen on respiration was marked in 20 cases. Attacks of vomiting and abdominal pain with elevation of temperature in children should demand a thorough examination by a physician, and the presence of any tenderness or rigidity in the right iliac fossa should at once demand the opinion of a surgeon. In all stages of acute appendicitis in children operation should follow immediately on diagnosis. The signs and symptoms may be slight, yet with very serious conditions in the abdomen.

OBSTETRICS

UNDER THE CHARGE OF

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Pregnancy Complicated by a Large Cyst of the Posterior Vaginal Wall.—FISCHER (*Monats. f. Geburts. u. Gynäk.*, 1912, xxxv, No. 4) reports the case of a multipara who came into spontaneous labor, and upon examination was found to have a large cyst of the posterior vaginal wall. The exact diagnosis of the condition occasioned some difficulty, labor ceased, and an attempt was made to deliver by forceps. During this attempt a rounded body was expelled from the vagina, which proved to be the cyst. The head was readily delivered so soon as the cyst had been removed. The cyst contained a yellowish fluid, and, upon examination, was found to be multiple, some of its compartments containing hair and yellowish material. This was composed of degenerated cells and fat. The wall of the cyst proved to be tissue resembling epidermis with papillary bodies. Hair bulbs were found in the epidermis.

Pregnancy Complicated by Prolapse of the Genital Organs.—SOLOMONS (*Jour. of Obstet. and Gyn. of British Empire*, March, 1912) reports two cases of extensive prolapse of the genital organs complicating pregnancy. The first was a multipara whose prolapse was so extensive that she was obliged to remain in bed during a previous pregnancy. Later, she came to the hospital three months pregnant, and again pessaries failed to give her relief. She was then operated upon by colporrhaphy; amputation of the cervix, shortening of the uterosacral ligament; perineorrhaphy was extensive; posterior colporrhaphy, and the Alexander Adams operation. This was done at the fourth month, and the patient's pregnancy proceeded without interruption, terminating in spontaneous labor with the birth of a well-developed child. In the second case, a multipara, the uterus completely prolapsed at six weeks and could not be retained by pessaries. At four months the patient had severe pain, with a temperature of 104° F. The cervix was edematous, ulcerated, and prolapsed. A diagnosis of septic infection was made, and it was thought that the uterus should be emptied. The patient was given 20 c.c. of antistreptococcic serum, and a very hot vaginal douche, followed six hours later by the discharge of a three and a half months' decomposing fetus. The placenta was adherent and removed with difficulty. The patient recovered. Solomons has collected the results of pregnancy in 26 patients in whom the uterus had been sustained by a vaginal suspension for prolapse; 21 of the 26 patients considered themselves cured by the operation, and many had passed through pregnancy successfully, retroversion returning in but 2 cases.

Laceration of the Vagina During Labor.—BJORKENHEIM (*Zentralbl. f. Gynäk.*, 1913, No. 8) from the clinic at Helsingbors reports the case of a multipara whose labor delayed so that the midwife in attendance called in a physician. The cervix was dilated, but the head was large and movable above the pelvic brim. The heart sounds were weak and irregular, and accordingly the forceps was applied. The instrument was removed and an attempt made to deliver by version, the midwife making strong pressure on the abdomen of the patient while the physician delivered the child. The head passed through the upper pelvis with great difficulty. There was fracture of the clavicle with dislocation of the cervical vertebra, and the child was dead born. Unfortunately, it was not weighed. In half an hour after the extraction of the child an effort was made to deliver the placenta by Credé's method. This failed, and the hand was introduced to remove the placenta, when the hand, following the cord, passed into a large cavity on the left side of the empty uterus. The placenta could not be found, but the hand passed through the opening into the abdomen among the intestines. The vagina was packed with gauze, and the patient brought by railway to the hospital. Upon admission, the general condition was fairly good, the patient was pale, but there was no fever, and the pulse was good. The umbilical cord was found passing to the left side of the vulva and thence through a large tear into the abdominal cavity. The placenta was very carefully drawn out by the cord, followed by dark blood. The patient was etherized, and abdominal section performed when the uterus was firmly contracted, but at the

side of the uterus there was a quantity of dark blood. In the space between the uterus and the bladder there was a tear in the peritoneum 10 cm. long, and the vagina was separated from the cervix through a distance of 6 cm., the opening communicating with the abdominal cavity. The parts were stitched together and a tampon of iodoform gauze placed in the parametrium through the vagina. The patient made, in the end, a good recovery, but this was complicated by pleurisy.

ZUBRZYCKI (*Zentralbl. f. Gynäk.*, 1913, No. 8) reports the case of a multipara in labor with strong pains, in whom the midwife discovered a tumor forming in the vulva. The physician who was summoned found, upon the left side of the vulva, a large elastic hematoma. Upon vaginal examination, it was observed that the tumor extended along the vaginal wall to the cervix, so that the lumen of the vagina was almost completely closed. The external os was dilated, the membranes ruptured, and the head of the child was in the pelvic cavity. During examination the tumor ruptured, discharging a mass of blood and blood clot. This was followed by very free hemorrhage. The child was immediately delivered by forceps, followed by the expulsion of the placenta, when the tumor was thoroughly irrigated, the bleeding vessels tied, and the cavity of the tumor drained with iodoform gauze. The patient's recovery was uninterrupted.

The reviewer, in a case in which a fruitless effort had been made to deliver by forceps, found a laceration of the vagina opening into the abdominal cavity sufficiently large to admit three fingers. The patient was delivered by the Porro operation, and the rent closed from above by a continuous catgut suture. Her recovery was uncomplicated, the torn vaginal tissue healing completely.

Pregnancy Complicated by Various Diseases.—In the *Annali di Ostetricia*, 1912, No. 4, PEZZINI and PIRANI report 27 cases of cholera complicating pregnancy. They find that pregnancy does not occasion any immunity against the cholera infection. The prognosis is not essentially altered by the pregnant condition, but becomes more grave the later in pregnancy cholera develops. The tendency to the interruption of pregnancy increases as pregnancy proceeds. The fetal mortality is very high, and the puerperal period does not seem to be greatly influenced by the disease. Where pregnancy is uninterrupted, and the patient survives cholera during the early months, the pregnancy may proceed to its normal termination.

An interesting case of echinococcus developing outside the peritoneum and behind the cervix is reported by GUSSAKOW (*Zentralbl. f. Gynäk.*, 1912, No. 28). The case had been mistaken by a physician for retroflexion of the pregnant uterus. The patient was kept under observation during pregnancy until labor developed, when she entered the hospital. The head of the child was above the entrance to the pelvic cavity, and the fetus in good condition. It was determined to open the posterior vaginal wall and endeavor to remove the tumor. Should this fail, abdominal section would be necessary. Upon incising the vagina, the tumor was opened and the characteristic echinococcus cysts removed. The tumor was reduced in size as much as possible, and labor proceeded with the mechanism characteristic of flat pelvis.

As labor pains were weak, three doses of pituitrin were administered during labor. The child was finally delivered by forceps, and although asphyxiated, recovered. The tumor cavity was packed with gauze, and the patient made a good recovery.

FRANZ (*Zentralbl. f. Gynäk.*, 1912, No. 28) has had good results in skin lesions occurring during pregnancy by the injection of a serum obtained from the blood of the umbilical cord. The patient was a primipara, aged nineteen years, who suffered from an eruption upon the skin of the abdomen, which itched violently, and spread upon the arms and legs. The lesions seemed to be multiple erythema with exudate; 20 c.c. of blood was taken from a vein, and 30 c.c. of serum two and one-half month's old, and obtained from the umbilical cord, was injected deeply into the right thigh. The temperature before and after the injection remained normal. The itching subsided when the eruption disappeared from the forearms. A fresh eruption appeared upon the left knee, and over other portions of the body characteristic spots developed. A second injection of 30 c.c. was given in the left thigh, followed by the disappearance of the exanthem from the abdomen and arms. The temperature and pulse remained normal. The eruption disappeared when labor developed with spontaneous birth and undisturbed recovery.

Glandular disease during pregnancy is the subject of a paper by RÜBSAMEN (*Archiv f. Gynäk.*, 1912, xcvi, No. 2). His first case was that of a primipara, aged sixteen years, with typical myxedema. Normal labor was followed by great improvement in the general condition, with a normal puerperal period. Thyroid extract seemed to be valuable in this case. A second patient was a primipara, aged thirty-two years, with cretinism, and contracted pelvis, delivered by section. The termination of pregnancy was followed by progressive improvement. The third case was a typical cretin, aged thirty-nine years. She was in the hospital for some time during her pregnancy, and showed great mental depression, with stupidity. The pelvis was highly contracted. After delivery by section, she improved very considerably. In four months after the operation, she was able to write plainly and was much better in general health. He gives the statistics of the clinic in Berne, where, among 718 patients, 34.2 per cent. had thyroid disease. He finds that after the classic operation on the thyroid, if this be done upon nulliparous patients, the tendency to the return of thyroid disease is less than if the patient had borne children before operation. He also describes, with photograph and x-ray illustrations, the case of a patient with substernal struma and twin pregnancy. The tumor was composed of two masses as large as a man's fist, with slight tremor in both hands, and some alteration in the eyes. The trachea and larynx were pressed upon by the tumor. Upon admission to the hospital, the patient's respiration was so labored that she could not lie down without difficulty. Upon coughing, the veins of the neck and chest became greatly distended. Viability was waited for, and the patient delivered as rapidly as possible by vaginal section, with lumbar anesthesia. It was found that twin fetuses were present, corresponding in development to the patient's menstrual history. The patient improved gradually after delivery.

GYNECOLOGY

UNDER THE CHARGE OF

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Palliative Treatment of Cervical Carcinoma.—An extremely simple form of treatment for inoperable cancer of the cervix, but one which is said to be extremely efficacious, is reported by BERZELLER (*Zentl. f. Gyn.*, 1913, xxxvii, 852). It consists merely in the application to the cervix of powdered sugar; the cervix is exposed in a cylindrical glass speculum, and wiped dry, the speculum is then half filled with the sugar, which is kept in place by means of an iodoform gauze pack. The treatment may be repeated from once a day to once a week according to the severity of the symptoms. Berzeller has found that its adoption is followed by a rapid disappearance of offensive odor and discharge, with a reduction in the amount of bleeding; the surface of the tumor becomes dryer, and the mass is reduced in size. In addition to these local improvements, there is often noted a general picking up in the patient's condition, due to lessened absorption of toxic products.

Hysterectomy by "Décollation Antérieure."—In cases of bilateral pyosalpinx, associated with extensive pelvic adhesions, the removal of the uterus by the method known as "décollation antérieure" is considered by BARNSBY (*Ann. mens. d'Obst. et de Gyn.*, 1913, ii, 449) "a truly marvellous operation." Originated by Faure, this procedure is especially indicated in those cases in which, after opening the abdomen, one comes upon a solid conglomerate of omentum, intestines, uterus, tubes, and ovaries, all fused into an indistinguishable mass, completely filling Douglas' pouch, and rendering the posterior surface of the uterus entirely inaccessible. In such cases, often the only definite landmark obtainable is the anterior surface of the uterus, or a portion of it. After ligating and cutting the round ligaments, and freeing any omental or intestinal adhesions to the anterior surface of the uterus (but disregarding all others) until the cervix is reached, the operator clamps, ties, and cuts the uterine vessels, and *then* cuts through the cervix *from before backward*. After cauterization and closure of the remaining cervical stump, the body of the uterus is drawn strongly upward, the adhesions to its posterior wall being at the same time carefully liberated. It is now a comparatively easy matter to perform that part of the operation which at first appeared so difficult—the removal of the adnexa, for as the uterus, turned completely upside down, is pulled up, the adnexa gradually free themselves owing to the unfolding of the two layers of the broad ligaments which takes place, following the uterus in its ascent. This leaves the utero-ovarian pedicle free in the fingers, to be clamped and cut; the adnexal masses, thus released, are easily drawn out and freed from their superior and lateral adhesions. In exceptionally bad cases it may be necessary to insert

the hand back of the adnexal mass in order to liberate this, a simple procedure when the line of cleavage is followed along the anterior wall of Douglas' pouch. One of the chief advantages of this operation in Barnsby's opinion, is the fact that the uterine vessels are tied before any attempt has been made to free the inflammatory masses; thus, in the later stages there is no hemorrhage to obscure the field and hamper the operator, nor is there any necessity of placing one clamp after another in friable tissue, in which they do not hold. It is usually possible, Barnsby has found, to remove the largest pus tubes without rupture by this method, but if an opening is inadvertently made into an abscess cavity or into the rectum, the unbroken diaphragm of adhesions above protects the general peritoneal cavity from infection.

Menstrual Molimina in Healthy Women.—The frequency and severity of subjective disturbances associated with the menstrual function in the normal young woman of average health are subjects upon which much has been said and written, but often without much basis of actual definite data, since such information is as a rule exceedingly difficult to obtain. Of considerable interest, therefore, are some investigations of CHISHOLM (*Journ. Obst. and Gyn. Brit. Emp.*, 1913, xxiii, 288), who has analyzed the records of 500 healthy girls and young women, aged from ten to twenty years, which were obtained at the routine physical examination required by a certain school. The purpose of these investigations were to determine the amount of conscious disturbance coincident to menstruation, the nature of such disturbance, and if possible its cause. Only about 16 per cent. of the girls had any lasting irregularity following puberty; in all the others, the function became regular within a comparatively few months after its onset. In almost 59 per cent. no disturbance of any kind was admitted as occurring at the menstrual period, in 14 per cent. there was very slight, occasional pain, and in 19 per cent. fairly constantly recurring pain, but so slight as to be little more than discomfort. In only 8 per cent. of the cases was there severe pain at each period, and in less than 2 per cent. was this so severe as to incapacitate the patient for a time. In those cases where pain was present, and of sufficient definiteness to be localized, it occurred in about 75 per cent. in the abdomen, the next most frequent site being the back. A few of the girls complained of headache, and other symptoms of general metabolic disturbance, such as vomiting, general lassitude, and malaise; nervous irritability was conspicuous by its absence. The local pain complained of was either aching or colicky in character, the former occurring especially frequently in a central position just below the umbilicus, and probably resulting from uterine congestion. Chisholm does not believe that the majority of menstrual disturbances are due to developmental abnormalities, since in many instances pain develops only some years after the commencement of menstruation, and must therefore be due to some subsequently developing condition. In only a little over 6 per cent. of the cases was there an undue profuseness of the flow. These girls did not appear to be below the average in general health, and the condition was in most instances relieved by having the patient stay at home for the first few days of each period. Chisholm has found that while, on the whole, the best developed girls are least

likely to suffer from menstrual disturbances, there is no very marked difference in this respect. In her experience, menstrual disturbances are not appreciably increased by hard mental work when this is carried on under healthy conditions, with plenty of opportunity for exercise and recreation, and she therefore does not altogether agree with the commonly accepted opinion that girls should be subjected only to the lightest mental activity, or should be kept from school altogether, during the time of puberty.

Heliotherapy in Gynecology.—AIMES (*La Gynécologia*, 1913, xvii, 129) says that in certain gynecological conditions much good may be accomplished by so simple a measure as exposing the body to the rays of the sun. He recommends the "sun bath" especially in cases of quiescent genital tuberculosis, but it is of value also in certain cases of chronic pelvic inflammatory disease, and of metrorrhagia. The technique consists merely in the exposure of the entire nude body if possible, if not, of the abdomen and pelvis, to the direct rays of the sun, starting with one or two sittings per day, of 5 minutes each, and gradually increasing this according to individual tolerance, until the patient can remain practically the entire day without discomfort. The head should always be well shaded. Aimes has found that as a rule patients who tan most quickly show the greatest amount of improvement. In addition to causing a general improvement in the bodily functions, increasing the appetite, reducing nervousness, and inducing restful sleep, the sun's rays appear to have a distinct antiphlogistic and hemostatic action, the cause of which has not as yet been determined. Often this form of treatment is advantageously combined with hydrotherapy.

OPHTHALMOLOGY

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The Central Light Sense and the Central Chromatic Sense in Chronic Glaucoma.—BEAUVIEUX AND DELORME (*Archiv. d'Ophthalmol.*, February, 1913, p. 93) have studied these perceptions in a considerable series of cases of chronic glaucoma. Such studies have heretofore yielded rather contradictory results, some holding the investigation of the light sense to be a valuable factor in diagnosis, while others regard failure of this sense as of common occurrence, being in fact a necessary accompaniment of lowered visual acuity or narrowing of the visual field from whatever cause. The study of the light sense includes two distinct factors: (1) the absolute or minimum perceptible,

(2) the differential, meaning thereby the minimum appreciable variation. Beauvieux and Delorme conclude that in chronic glaucoma the differential light sense is affected first; it is diminished at a time when the ophthalmoscopic lesions are but little marked. Such diminution is quite independent of lowered visual acuity or narrowing of the visual field. It is, on the contrary, intimately linked to the state of the intra-ocular tension. Variations of the absolute light sense: this function becomes affected only in advanced chronic glaucoma when the disk is already cupped. Such alteration in the absolute light sense is intimately connected with the optic atrophy which accompanies glaucomatous excavation. It does not depend upon the acuity nor upon the visual field; neither is it influenced to an appreciable extent by subsequent regulation of the tension through treatment, inasmuch as the optic atrophy upon which it depends is a definite lesion. Modification of the color sense: the color sense is usually normal in all cases where the absolute light sense is intact. When optic atrophy has begun disturbances of color perception are not rare. Differential diagnosis: considerable diminution of the differential light sense with entire preservation of the absolute light sense has been found by Beauvieux and Delorme to occur besides in glaucoma only in papillary stasis (choked disk). In optic atrophy, the absolute light sense is affected first, the differential sense only suffers after the ophthalmoscopic lesions are clearly pronounced. Then also disturbances of the color sense become the rule. Prognosis: normal light sense, absolute and relative, indicate integrity of the fibers of the optic nerve. The prognosis is probably best in those cases where the differential light sense is raised after instillation of pilocarpin. It is also very favorable even if amelioration does not follow the use of miotics but comes on after (Lagrange's) operation. Beauvieux and Delorme are inclined to think that the prognosis should be reserved in cases where the alteration in the differential light sense persists even after the tension has become normal.

Treatment of Divergence by Overcorrecting Concave Lenses.—H. LANDOLT (*Klin. Monatsbl. f. Augenheilk.*, January, 1913, p. 47) has obtained cure in cases of both exotropia and exophoria by the use of overcorrecting concave lenses. In one case of alternating divergent strabismus of high degree with emmetropic refraction and full vision in each eye, double tenotomy with subsequent prismatic and stereoscopic exercises was unavailing. Concave lenses of 6D before each eye gave instant orthotropia. The divergent strabismus became transformed into insufficiency of convergence. The minus lenses were employed for daily exercise; finally binocular vision was reestablished even when the lenses were omitted. In a second case of high degree of insufficiency of convergence in a myope of 2D in both eyes with full vision, correcting glasses combined with 4 degree prisms base had but slight effect upon the exophoria; -3.5D without prisms gave entire relief. Both of these patients were young as must necessarily be the case. Landolt explains this effect of overcorrecting concave glasses as a logical deduction from that of convex lenses in the relief of convergent squint: The stimulus to increased accommodation

calls forth an augmented impulse to convergence also. This effect, as well as the opposite in the case of convergent lenses, can be readily demonstrated by holding a concave lens before a youthful emmetropic eye; excessive convergence immediately takes place. The reporter observes that no ill effects need be apprehended from the use of such glasses, it having been demonstrated that myopia is not caused by the accommodation, and that with present-day views, more is to be feared from undercorrection than overcorrection of myopia.

Brawny Scleritis.—In 1907 Schlodtmann described from Fuch's clinic under the term "brawny infiltration of the sclera and conjunctiva" a type of anterior scleritis which presented distinctive clinical features. Since this publication histological findings in 11 additional cases have been published. Tuberculosis, syphilis, and rheumatism have on clinical grounds apparently been excluded as etiological factors, and the cause of the condition has remained obscure. VERHOEFF (*The Ophthalmoscope*, January, 1913, p. 2) reports a case which came to histological examination, in which a positive Wassermann reaction was obtained. He concludes that "Brawny Scleritis is a distinct type of scleritis, differing essentially in both its clinical and histological aspects from anterior Nodular Scleritis. Clinically, it is characterized by the advanced age at which it occurs (usually over sixty), its insidious onset and extremely chronic course, and the diffuse congestion and thickening of the sclera and episclera without the formation of definite nodules. The infiltrated recti tendons, however, may simulate sclerotic nodules. Ultimately, the anterior part of the sclera becomes involved around its entire circumference and the process also invades the cornea. Evidences of intra-ocular involvement, such as vitreous opacities and iritis, occur late and are relatively slight. Pain likewise does not occur until late. The intra-ocular pressure is normal or elevated. Both eyes are usually affected, although not always simultaneously, and the disease usually leads to blindness in one eye at least. Histologically, in the early stages there is a diffuse plasma cell infiltration of the sclera and episclera. Later, or possibly at the same time, the sclera becomes pervaded by granulation tissue, the plasma cell infiltration increases and involves by continuity, first, the anterior part of the choroid and ciliary body, and finally, the whole uvea. Necrosis of the granulation tissue takes place, showing itself as areas of purulent infiltration containing numerous endothelial phagocytes filled with fat, or as well marked caseation. Giant cells may or may not be numerous. Periarteritis and endarteritis are marked in the affected tissues. Even in the advanced stages, where there is intense infiltration of the ciliary body, there is no formation of cyclitic membrane. Separation of the retina ultimately occurs, due to exudation of serum from choroid. The character of the lesions in Brawny Scleritis strongly indicates a syphilitic origin for the affection. This is also indicated by a positive Wassermann reaction obtained in Verhoeff's case, but until such reactions have been obtained in a number of cases, or spirochetes have been demonstrated in the lesions, it cannot be regarded as absolutely established that Brawny Scleritis is a manifestation of syphilis."

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Fibrinemia.—J. O. WAKELIN BARRATT (*Jour. Path. and Bact.*, 1913, xvii, No. 3) has published an interesting article describing his attempts to find the cause of death when hemoglobin solution is injected into the blood stream. It has been known that a solution of hemoglobin from red blood cells of a rabbit, if injected in sufficient amount into the ear veins of another rabbit, would cause dyspnea, convulsions, and finally death. The fatal result is not supposed to be due to dissolved hemoglobin, but to substances derived from the stroma of the red blood cell. Morawitz, who some years ago advocated the transfusion of defibrinated blood in cases of anemia, recommended that such blood should be kept for some time before injection, so that the fibrin ferment might be modified to an inert substance; such precaution, nevertheless, was not always successful. It has been further observed that the fatal symptoms occur even if the serum was obtained from the animal in which the injection was made. Barratt first directed his attention to finding out if red blood cells laked by the addition of distilled water yielded thrombokinase, which he was able to answer in the affirmative. He was further able to determine that the thrombokinase thus supplied, comes almost if not entirely from the red blood cells; the solution of hemoglobin, therefore, whether in the form of laked red cells, or of supernascent liquid contains thrombokinase. If thrombokinase itself be injected, fibrin is separated slowly, which blocks the smaller bloodvessels, and can be found in the bloodvessels of the lungs; this can also be seen when thrombin is injected. The separation of fibrin in all cases is due to the action of thrombin, and according to the rapidity with which thrombin is formed, clotting occurs in the heart and the great bloodvessels, or in the capillaries, the latter being the case if the separation of fibrin occurs slowly. The symptoms produced appear to be entirely the result of mechanical interference with the circulation, and Barratt was able to find no evidence of a toxic effect produced by the fluid injected.

Secondary Infection in Pulmonary Tuberculosis.—AVERY and LYALL (*Jour. Med. Research.* 1913, xxviii, No. 1) deal with the subject of secondary infection and its importance in pulmonary tuberculosis. They point out that there are three schools whose opinions differ upon this subject. They first consider that mixed infection plays no essential part in the progress of the disease, a view held by v. Leyden, Straus, Fraenkel, and others; the second group, among which are to be found adherents of the Koch school, Cornet, and others, considers that the lesions and the more severe symptoms of pulmonary tuber-

culosis are due to the secondary and not to the primary infection; the third school, in which are Baldwin, Marmorek, and Römer, considers that the lesions and symptoms may be caused by the tubercle bacillus alone, but in many cases severe symptoms and unfavorable progress are due to secondary infection. Necessarily in such a division of opinion, it is essential to closely define terms, and it may be said that most observers consider that the organisms which are accidental incomers from the air are not properly to be considered as secondary infecting agents, unless they actually invade the blood or the tissues. Avery and Lyall point out that some of the Koch school have receded from their first position, being compelled to recognize that the tubercle bacillus alone is able to cause fever, and that destruction of lung tissue can be brought about without the assistance of secondary infection. Baldwin and Marmorek have shown the power of the tubercle bacillus to cause lesions quite unaided by any other microbe, but on the other hand, such lesions progress more rapidly and more dangerously in the presence of secondary infections. Avery and Lyall examined very carefully the sputum of 5 bronchiectasis cases, and of 15 cases of pulmonary tuberculosis, isolating and identifying the organisms present. The bacteria found differed so little from those reported by Hastings and Niles in non-tuberculous diseases of the respiratory tract, that they felt it impossible to draw useful inferences from this part of the investigation. They made blood cultures in 5 cases of bronchiectasis, and 110 cases of pulmonary tuberculosis, of which 38 were far advanced in the disease; in no case were they able to demonstrate a secondary bacteriemia.

Chemical and Serum Therapy in Pneumococcus Infections.—

ENGWER (*Zeit. f. Hygiene u. Infek.*, 1912, lxxiii, Heft 2) has experimented with infective doses of varying strength of pneumococcus, and attempted to meet the disease by combinations of chemical and serum therapy; he has attained a certain degree of success. He has used a solution in oil of ethylhydrocuprein and finds it effective in pneumococcus infection of the mouse and the guinea-pig; while with certain degrees of infection all the control animals died, he was able to save a certain number of animals by treatment. His best results were obtained by a combination of this chemical therapy with the usual serum therapy, although under certain circumstances the two appear to be antagonistic instead of mutually helpful. Throughout the experiments some animals were found to be poisoned by the chemical, and such fatal results appeared to be greater in cold weather. Engwer considers that the action of the drug depends upon the actual destruction of the pneumococci outside the cells rather than upon any action obtained by phagocytosis.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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THE
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ORIGINAL ARTICLES

THE PATHOLOGY OF THE THYROID GLAND IN EXOPHTHALMIC GOITER.¹

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THE studies on which the present paper is based are a continuation of those first reported to the Association of American Physicians five years ago.² At that time, I gave a detailed analysis of the pathological examination of 259 thyroids, removed from patients listed as "exophthalmic goiter" in the Mayo Clinic from January 1, 1905, to May 10, 1908, and in addition a review of the pathological reports on 35 cases similarly listed in the Mayo Clinic prior to January 1, 1905. While these cases were not all such as we would now diagnosticate exophthalmic goiter, they were all toxic, and probably contained as high a percentage of cases of true exophthalmic goiter as could have been found in any clinical list at that time.

The solution of problems of the pathology of the thyroid has long been rendered more difficult by indefinite clinical diagnoses and nomenclature, and this no doubt accounts for much of the disagreement between workers in different clinics. While non-toxic cases usually have been diagnosticated clinically "simple goiter," and cases with marked symptoms have been diagnosticated "exophthalmic goiter," yet many cases with mild symptoms have also been called "simple goiter," and many cases, though not

¹ Presented before the Association of American Physicians, Washington, D. C., May 7, 1913.

² Wilson, AMER. JOUR. MED. SCI., 1908, cxxxvi, 588 to 605.

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true exophthalmic, yet markedly toxic, have been called by most clinicians "exophthalmic goiter."

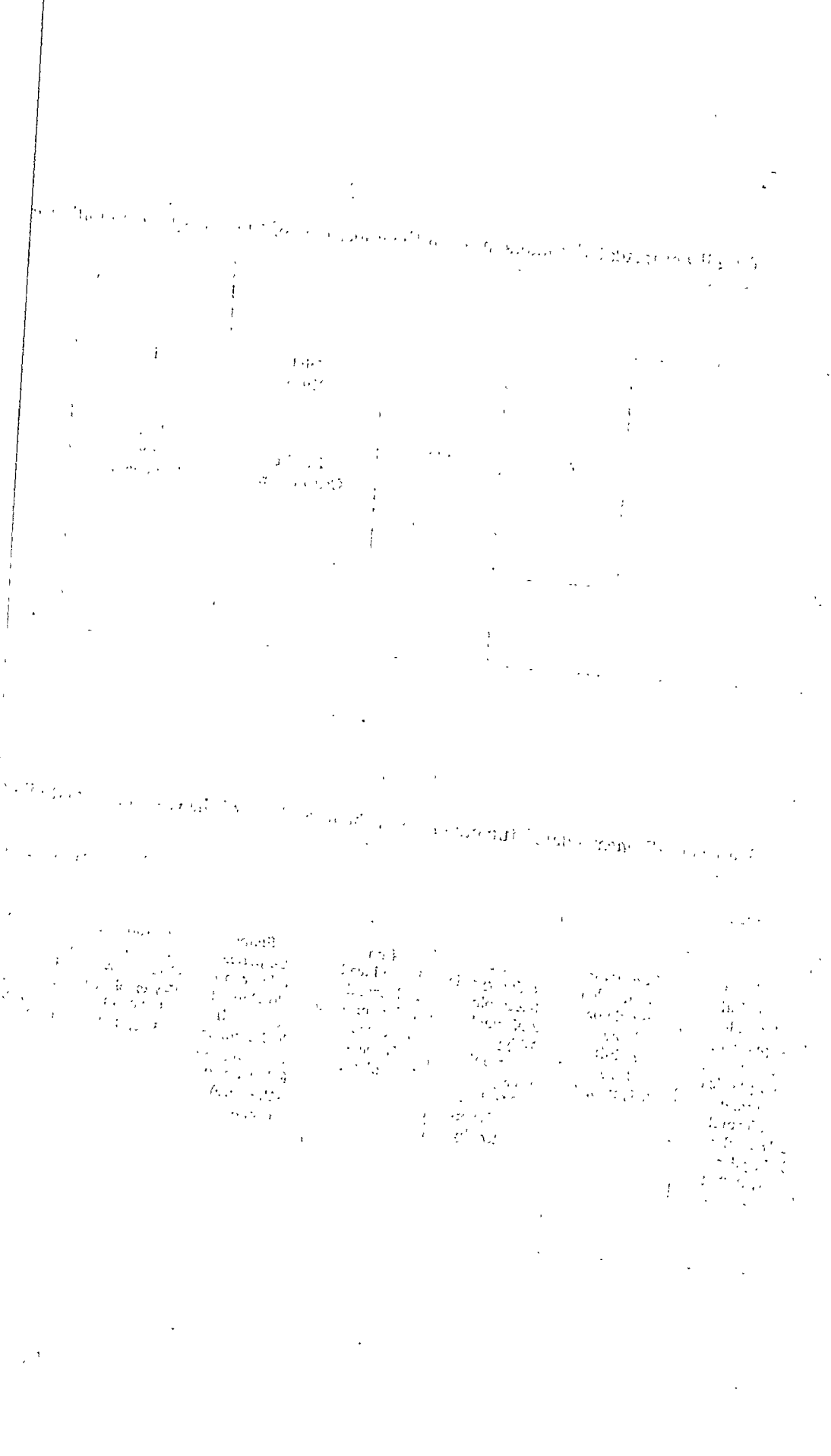
Though a sharp distinction between the two clinical types of toxic cases—exophthalmic and non-exophthalmic—had not been made in 1908, I was able to show that pathologically there were two distinct types of glands to be found among thyroids removed from toxic goiter cases. While purposely avoiding as much as possible previously used technical terms, I attempted to simplify our conception of the pathology by pointing out that the essential element in a large percentage of the cases was an increase in the amount of working tissue—parenchyma cells—within the previously formed acini, or, in other words, hypertrophies, hyperplasias, and regenerations, while in a smaller percentage of the cases there was an apparent increase in the amount of working tissue—parenchyma—due to an increase in the number of acini, or, in other words, adenomas, adenomatoses, etc. Class I, containing the hypertrophies, hyperplasias, and extreme regenerations, constituted 79 per cent. of the total number of specimens examined, while Class II, containing the fetal and colloid adenomas, the adenomatoses and the so-called simple colloid thyroids, constituted 21 per cent. of the specimens examined.

In comparing my theoretical estimate of the stage and severity of the disease as indicated by the above data with the clinical facts as previously observed and noted by Plummer, it was shown that a direct relationship existed between the apparent functional activity of the gland and the stage and severity of the clinical symptoms. In reviewing the clinical data of his more recent cases, Plummer³ has found that practically all, if not all, of the cases of clinically true exophthalmic goiter lie in the pathological groups showing hypertrophy and hyperplasia, while the toxic non-exophthalmic cases are scattered among the other pathological groups. We have, however, up to the present time, continued the ordinary method of listing clinically all severe toxic goiter cases closely resembling exophthalmic cases⁴ on the "exophthalmic goiter" list, while on the "simple goiter" list are placed those cases in which there are slight or no acute toxic symptoms. Our "exophthalmic goiter" list therefore contains those cases coming to our clinic which are ordinarily diagnosticated exophthalmic goiter, but which Dr. Plummer divides clinically into two classes, exophthalmic toxic, and severe non-exophthalmic (*i. e.*, non-hyperplastic) toxic.

I have recently reviewed all the gross and microscopic fixed tissue at hand from the cases reported in 1908, and, in addition, have studied grossly and microscopically in fixed tissues all the glands available which have been removed between May 10, 1908, the date of my previous report, and January 1, 1913, from all patients

³ AMER. JOUR. MED. SCI., 1913, cxlvi, 790.

⁴ Plummer, *loc. cit.*



on our "exophthalmic goiter" list. This includes a total of 1208 thyroids from patients all of whom had shown marked toxic symptoms, though not all of whom, in the light of our present clinical knowledge, would now be diagnosticated true exophthalmic goiter. In addition to these 1208 glands from toxic cases, I have similarly studied the glands removed during the year 1912 from cases grouped clinically as "simple goiters," 585 in all. These latter 585 thyroids are from patients presenting very slight or no acute toxic symptoms. I have further studied the thyroids from a number of human embryos and from children, adolescents, and adults coming to autopsy without clinical history of thyroid derangement. My observations on the latter groups will be presented in later papers.

In order to maintain a standard of comparison in the analyses of these cases, it has been found necessary to adopt numerical equivalents for amount, size, degree, etc., and the analytical data thus designated has been tabulated on forms parallel in size and arrangement of names with those used by Plummer for the tabulation of the clinical data. The headings of the tables are shown in Table I.

All pathological observations have been made wholly independently of the clinical observations and not compared with the latter until the entire series was completed.

While many thyroids may each present a great variety of histological pictures, yet a careful examination of a large number of sections from blocks of fixed tissue from different areas combined with the examination of the gross specimens permits one to classify the glands with considerable definiteness. In grouping the specimens, I have classified them with but slight change on the basis which I adopted in 1908 and elaborated last year.⁵ Thus groups A, B, C, and D represent Class I, namely; the parenchymatous hypertrophies and hyperplasias and extreme regenerations, while groups E, F, G, and H represent Class II, namely, the "adenomas," "adenomatoses," and "colloid goiters."

Hypertrophy and hyperplasia are almost always intermingled, but it is possible to subdivide the hypertrophies and hyperplasias into three classes: Group A, early primary parenchymatous hypertrophy and hyperplasia (see Fig. 1); Group B, active advanced primary parenchymatous hypertrophy and hyperplasia (see Fig. 2); Group C, regressing primary parenchymatous hypertrophy and hyperplasia (see Fig. 3). I have used the term "primary" in each of these classifications because I believe it represents a stage of hypertrophy and hyperplasia developing in parenchyma which previously has not been markedly atrophic. Group D contains those specimens in which a marked regeneration of parenchyma is found developing on apparently previously atrophic parenchyma

⁵ Wilson, *Northwest Medicine*, Seattle, Washington, 1913, v, 1 to 5.

lining the walls of previously distended, colloid-filled acini (see Fig. 4). This regeneration is marked by the presence of numerous minute acini lined with low spherical or cuboidal epithelium and filled quite early with densely staining colloid. Critically con-

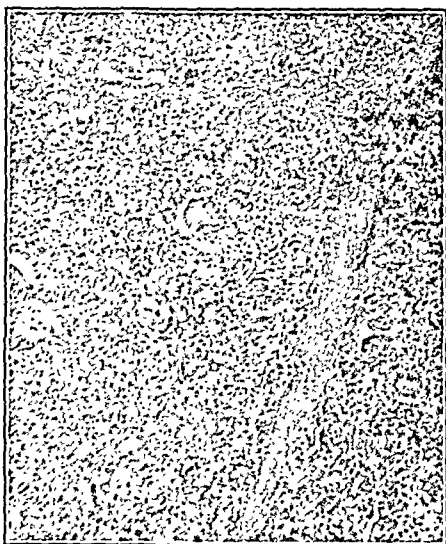


FIG. 1.—Photomicrograph of a section of thyroid. $\times 120$. Type A. Early primary parenchymatous hypertrophy and hyperplasia. From a case of clinically early true exophthalmic goiter.

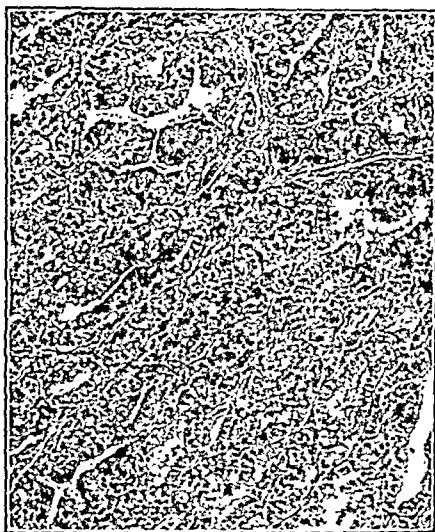


FIG. 2.—Photomicrograph of a section of thyroid. $\times 120$. Type B. Advanced primary parenchymatous hypertrophy and hyperplasia. From a case of clinically severe true exophthalmic goiter.



FIG. 3.—Photomicrograph of a section of thyroid. $\times 120$. Type C. Regressing primary parenchymatous hypertrophy and hyperplasia. From a case of clinically true exophthalmic goiter, late stage.



FIG. 4.—Photomicrograph of a section of thyroid. $\times 120$. Type D. Secondary regeneration of atrophic parenchyma. From a case of clinically toxic non-exophthalmic goiter.

sidered, the process is really a form of hyperplasia, and it is possible indeed for it to progressively grade over into primary hypertrophy and hyperplasia, but I have rigidly excluded from groups A, B, and C all glands which did not show marked infolding of acinar walls

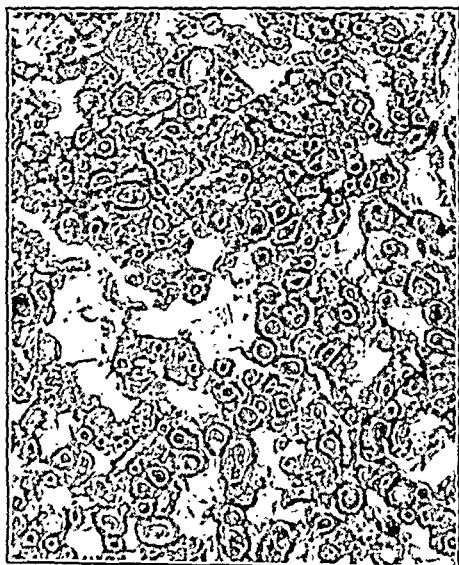


FIG. 5.—Photomicrograph of a section of thyroid. $\times 120$. Type E. Fetal adenoma. From a case of clinically toxic non-exophthalmic goiter.



FIG. 6.—Photomicrograph of a section of thyroid. $\times 120$. Type F. Degenerating fetal adenoma. From a case of clinically toxic non-exophthalmic goiter.



FIG. 7.—Photomicrograph of a section of thyroid. $\times 120$. Type G. Adult, "colloid" adenoma. From a case of clinically toxic non-exophthalmic goiter.



FIG. 8.—Photomicrograph of a section of thyroid. $\times 120$. Type H. "Colloid thyroid." From a case of clinically non-toxic goiter.

lined with columnar epithelium. On the other hand, it is frequently impossible to draw the line between those degrees of regeneration in a colloid thyroid which might fairly be presumed to be the cause of toxic symptoms and those in which no effect can be noted. All that I have attempted here is to note in a study of the glands removed from known toxic cases the presence or absence of marked regeneration. While theoretically it would seem to be extremely confusing to differentiate secondary regenerations from primary hypertrophies and hyperplasias, yet, as a matter of fact, when sections from material which has been properly fixed and stained are studied, the task is not a difficult one.

Of the groups in Class II, group E contains the actively growing, non-degenerating fetal adenomas (see Fig. 5); group F contains fetal adenomas which show any of the several types of degeneration—myxomatous, hyaline, calcareous, etc. (see Fig. 6); group G contains those definitely encapsulated adenomas whose acini are too large to be classified as fetal and which may or may not be degenerated (see Fig. 7); and group H contains those thyroids not included in the previous classes, many of which, though not presenting definitely encapsulated tumors, yet are composed of more or less segregated groups of acini presenting a picture which, following Adami's lead, I prefer to class as "adenomatoses" (see Fig. 8).

The accompanying table gives the classification of the thyroids studied according to the above grouping.

A study of the table reveals the following interesting points:

1. Approximately four-fifths, 79 per cent., of all thyroids from patients who had exhibited sufficiently severe acute toxic symptoms to warrant the clinician in placing them on the "exophthalmic goiter" list, showed marked hypertrophy or hyperplasia, or, more usually, both.

2. During the year 1912 this percentage arose to 89. At the same time, a parallel examination by the same observer of 585 thyroids from patients on the "simple goiter" list for 1912 showed but four cases—less than 1 per cent.—with hypertrophy and hyperplasia. Of these four cases, three were children and one was a young adult female whose lack of toxic symptoms can be accounted for only on the hypothesis that she was highly resistant and had not yet had time to be affected.

3. During the years 1911 and 1912 every patient diagnosticated clinically as true exophthalmic goitre and on whom thyroidectomy was done, furnished thyroid tissue which pathologically was placed in the groups marked A, B, or C, that is, showing primary parenchymatous hypertrophy and hyperplasia.

4. So far as can be determined none of the 133 patients—11 per cent.—whose thyroids showed only secondary regeneration of atrophic parenchyma would now be classified clinically according

to Plummer as true exophthalmic goiter. This distinction is clinically sharp and positive for the years 1910, 1911, and 1912, and not yet critically reviewed from the clinical standpoint for the preceding years.

5. The statement in paragraph 4 is equally true for the 130 cases—10 per cent.—whose thyroids are grouped as E, F, G, or H (adenomas, etc.).

6. At the same time these groups D, E, F, G, and H—regenerations, adenomas, colloids, etc.—contain 97 per cent. of all thyroids removed from patients on the "simple goiter" list for 1912.

TABLE II.—PATHOLOGICAL CLASSIFICATION OF THYROIDS FROM PATIENTS ON "EXOPHTHALMIC GOITER" LIST FROM JANUARY 1, 1905, TO JANUARY 1, 1913, AND OF THYROIDS FROM PATIENTS ON "SIMPLE GOITER" LIST FOR 1912.

"Exophthalmic Goiter" List.										"Simple Goiter" List.	
	Years . . .	1905	1906	1907	1908	1909	1910	1911	1912	Totals	1912
A	Early primary parenchymatous hypertrophy and hyperplasia.	...	1	4	2	1	3	15	6	32 3%	.. A
B	Advanced primary parenchymatous hypertrophy and hyperplasia.	4	26	35	41	44	68	108	89	415 34%	1 B
C	Regressing primary parenchymatous hypertrophy and hyperplasia.	7	21	44	55	46	78	107	140	498 41%	3 C
	Total hypertrophy and hyperplasia (A + B + C).	11 69%	48 83%	83 68%	98 69%	91 71%	149 77%	230 81%	235 89%	945 79%	4
D	Secondary regeneration of atrophic parenchyma of "colloid" goiter.	1 6%	3 5%	24 20%	24 17%	17 13%	30 15%	20 7%	14 5%	133 11%	50 9% D
E	Fetal adenomas.	1	3	7	17	8	2	12	2	52 4%	35 E
F	Degenerating fetal adenomas.	3	3	5	3	5	12	21	10	62 5%	101 F
G	Adult ("colloid") adenomas.	...	1	1	...	6	1	...	3	12 1%	128 G
	Total adenomas (E + F + G).	4 25%	7 15%	13 11%	20 14%	19 15%	15 7%	33 12%	15 6%	126 10%	264 44 %
H	Atrophic parenchyma ("colloid") thyroids, "adenomatoses," etc.	1	...	1	2	4	259 44 %
	Malignant tumors.	8 1½%
	Total number of thyroids	16	58	121	142	128	196	283	264	1208	585

In attempting to estimate from the pathological data alone the stage of the toxic clinical symptoms, the following factors have been taken into account: (1) Age of the patient, (2) weight of the portion of gland removed, (3) character of the bloodvessels, (4) amount of stroma, (5) size and shape of the acini, (6) amount of hypertrophy and hyperplasia of the parenchyma cells, and (7) amount and density of the secretion contained within the acini. These factors

must all be considered in estimating the product and output of the gland so far as may be made from a pathological examination of the tissues. A careful consideration of all these factors has been made in each case examined and a tentative estimate given of the stage and severity of the disease at the time the patient was operated on. These estimates have been compared in parallel columns with the clinical estimates made by the examining physician for all cases operated on during 1910, 1911, and 1912 (the only years for which the full clinical data, except of those given in my paper of 1908, have as yet been critically reviewed). The results may be briefly summarized as follows:

1. Of the 24 cases diagnosticated pathologically as Group A (early primary parenchymatous hypertrophy and hyperplasia), 21 (87.5 per cent.) had exhibited symptoms for but three months or less.

2. Of the 265 cases placed pathologically in Group B (advanced primary parenchymatous hypertrophy and hyperplasia), 11 (4 per cent.) gave a history of toxic symptoms for but three months, 155 (58 per cent.) from three months to one year, 34 (13 per cent.) (almost all young individuals) slightly over a year, but with a ligation shortly preceding thyroidectomy, while 65 (24.5 per cent.), these again almost all young individuals, had exhibited symptoms for over a year and had had no ligation previous to thyroidectomy.

3. Of the 325 cases diagnosticated pathologically as group C (regressing primary parenchymatous hypertrophy and hyperplasia), 8 (2 per cent.) gave a history of but three months' duration of symptoms (and without ligation prior to thyroidectomy), 25 (8 per cent.) gave a history of one year or less duration of symptoms (and without ligation prior to thyroidectomy), while the remainder, 292 (90 per cent.), gave clinical histories of more than one year's duration or had had a ligation some weeks before the performance of thyroidectomy.

Thus it will be seen that notwithstanding the inaccuracies of patients' statements as to the duration of symptoms, notwithstanding the confusing factor of a ligation previous to thyroidectomy, and notwithstanding the difficulties of correctly estimating the total function from an anatomical study of but a portion of a gland, the fact remains that the stage of true exophthalmic goiter can be estimated with considerable accuracy from the pathological data alone in about 80 per cent. of all cases examined.

In attempting to estimate the severity of the toxic symptoms in the cases with true exophthalmic goiter, all of which had shown pathologically some stage of hypertrophy and hyperplasia in the thyroid (Groups A, B, or C), the same factors were taken into consideration as those entering into the estimate of the stage of the disease. A careful consideration of these data resulted in the classification of the cases for 1910, 1911, and 1912 into the four

grades of severity: (1) Very mild, (2) moderate, (3) severe, (4) very severe. On only 542 cases out of the 614 was it possible to make a definite comparison of the estimated severity from the pathological standpoint with the severity as noted by the clinician just prior to thyroidectomy.

Out of these 542 cases, 29 were estimated pathologically as "1," or of "mild" severity. Twenty-two out of the 29 had been previously similarly grouped by the clinician, or, in other words, the pathological estimate agreed with the clinical findings in 76 per cent. of the cases in this group.

Of the 306 cases estimated pathologically as "2," or of "moderate" severity, 235 were similarly placed by the clinician, an agreement of 77 per cent. in this group.

Of the 166 cases estimated as of severity "3," that is "severe," 117 were similarly grouped by the clinician, an agreement of 70 per cent.

Of the 41 cases estimated pathologically as severity "4," that is "very severe," 33 have been similarly grouped by the clinician, an agreement of 80 per cent.

Thus of the 542 cases on which the degree of severity was estimated from the examination of pathological specimens, such estimate agreed with the clinical estimate in 407 cases, or a total pathological accuracy of 75 per cent.

CONCLUSIONS. 1. A detailed pathological study of fixed tissue preparations from 1208 thyroids, removed from patients whose condition would ordinarily have been diagnosticated exophthalmic goiter, showed that 79 per cent. of the thyroids contained large areas of marked primary hypertrophy and hyperplasia. A parallel clinical study has shown that for a period of three years all cases with true exophthalmic goiter, and from whom gland tissue was removed, fall into this list.

2. In the above series of 1208 so-called "exophthalmic goiters" plus 585 so-called "simple goiters," or a total of 1793 thyroids, but 4 instances of marked primary hypertrophy and hyperplasia of the parenchyma have been noted in cases which did not show clinical symptoms of true exophthalmic goiter. Three of these four patients were children.

3. Twenty-one per cent. of the 1208 glands studied were either regenerations or adenomas. Clinically, while all of these were markedly toxic, all were chronic and none of them would now be grouped clinically as true exophthalmic goiter.

4. By assuming that the symptoms of true exophthalmic goiter are the results of an excretion from the thyroid, and by attempting to determine the amount of such excretion from the pathological data, one is able to estimate in a large series of cases the clinical stage of the disease with about 80 per cent. of accuracy

and the clinical severity of the disease with about 75 per cent. of accuracy.

5. It would therefore appear that the relationship of primary hypertrophy and hyperplasia of the parenchyma of the thyroid to true exophthalmic goiter is as direct and as constant as is primary inflammation of the kidney to the symptoms of true Bright's disease. Any considerable finding to the contrary I believe to indicate either inaccurate or incomplete observations on the part of the pathologist or clinician, or both.

THE CLINICAL AND PATHOLOGICAL RELATIONSHIP OF SIMPLE AND EXOPHTHALMIC GOITER.¹

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Up to January 1, 1909, 1004 operations had been done on 966 cases of goiter at St. Mary's Hospital. A brief review shows that we were classifying the cases as simple and exophthalmic goiter. We recognized that a considerable percentage of cases of so-called simple goiter had constitutional symptoms. Whether or not the cases having constitutional symptoms were placed on the simple or exophthalmic list depended upon how closely the clinical complex approached the well-known picture of Graves' disease.

Wilson, in 1908, after reviewing the available pathological material from the cases that had been diagnosed exophthalmic goiter, pointed out that 80 per cent. of the glands showed hyperplastic changes, and that in general the length and severity of the case history could be pointed out from the pathological findings. While it was impossible to overlook the fact that the tissue removed from the majority of patients having a well-developed picture of Graves' disease was hyperplastic, we could not come definitely to the conclusion that this evidence of activity on the part of the thyroid was a constant finding in exophthalmic goiter as long as 20 per cent. of the cases so diagnosed did not show this change in the thyroid.

At about this time a review of the clinical histories and pathological findings of the entire series listed as simple and exophthalmic goiters led to the following tentative conclusions: (1) that at least two distinct but similar types of thyroid intoxication exist one associated with non-hyperplastic goiter, the other with hyperplastic or hypertrophic thyroid; (2) that exophthalmos

¹ Read before the Congress of American Physicians, Washington, May 6, 1913.

should be noted only in cases having hyperplastic or hypertrophic thyroids; (3) that the failure of our statistics to show the above conclusions was due largely to the following errors: (a) accepting the clinical findings and diagnosis of exophthalmic goiter for all cases placed on the exophthalmic goiter list; (b) accepting the pathological findings from only a portion of one lobe of the thyroid; (4) that the clinical errors were attributing the tremor, tachycardia, etc., of neurasthenia, cardiovascular and nephritic diseases to the thyroid and noting the existence of exophthalmos when only a Stellwag's sign and naturally prominent eyes are associated with the thyrotoxicosis of non-hyperplastic goiter.

I have from time to time pointed out in discussions, statistical data bearing out the above conclusions, but have refrained from publication until going into a wealth of confusing detail to explain the apparent exceptions is unnecessary.

In writing the histories of the 3207 cases that have come to operation since January 1, 1909, forms were used covering the points which might later prove of interest. Figures and signs having, insofar as possible fixed values, were used in place of descriptive adjectives. Observations of facts and opinions were carefully distinguished. The clinical and pathological findings were placed in parallel columns without any comparison of notes on the part of the clinicians and pathologists. This made possible the compilation of statistics by clerks who were not in any way warped by preconceived ideas or a knowledge of factors other than those under immediate consideration.

The term thyrotoxicosis is here applied to the constitutional state associated with goiter. As a matter of convenience for quickly presenting the association of the clinical and pathological findings, the constitutional symptoms accompanying goiter were attributed to a toxemia, the result of a disturbed thyroid function. As a temporary expedient the cases were classified pathologically as hyperplastic and non-hyperplastic, and clinically as hyperplastic-toxic, hyperplastic atoxic, non-hyperplastictoxic, and non-hyperplastictoxic. The glands showing marked hypertrophy were included with the hyperplastic goiters. Following this classification for the 2917 new cases coming to operation between January 1, 1909, and January 1, 1913, 42.8 per cent. were hyperplastic and 57.2 per cent. were non-hyperplastic. Of the hyperplastics 99.2 per cent. were toxic and 0.8 per cent. were atoxic. Of the non-hyperplastic 23.3 per cent. were toxic and 76.7 per cent. were atoxic.

While the association of the constitutional symptoms with non-hyperplastic goiter was to a certain extent a personal equation, this was to a limited degree true for the cases having hyperplastic thyroids. The estimation that 23.3 per cent. of the non-hyperplastic goiters were toxic was made on a conservative basis.

Patients coming under observation with non-hyperplastic toxic goiter gave a history of having first noted the goiter at the average age of 22 years, and the evidence of intoxication at the average of 36.5 years. The corresponding ages for hyperplastic goiter were respectively 32 and 32.9 years.

That non-hyperplastic goiter was noted 10 years earlier in life than hyperplastic goiter, that 14.5 years elapsed between the appearance of non-hyperplastic goiter and the development of notable toxic symptoms, and that the constitutional symptoms were noted but a few months later than the goiter in the patients affected with hyperplastic thyroid was alone sufficient to show that we were dealing with at least two distinct pathological and clinical groups. That one was not the sequence of the other was self-evident.

Are all hyperplastic goiters coming to operation toxic? Throughout the series the number of cases in which the clinician failed definitely to note and attribute constitutional symptoms to the thyroid and which were later diagnosed by the pathologists hyperplastic thyroid varied from 2 cases in 1909 to 4 cases in 1912; 2 of these 4 cases were in children under 4 years of age and could be excluded in considering the hyperplasia of adults. The third case was a girl, aged 15 years, who gave a history of having noticed the goiter, periods of tremor, tachycardia, and palpitation for nine months. However, these symptoms were not attributed to the thyroid previous to operation. The fourth case was a woman, aged 47 years, who gave a history of having noticed the goiter for twelve years, rapid growth during the few months previous to coming to operation and a long train of symptoms, part of which might be attributed to thyroid intoxication. A few cases that had small areas of hyperplasia in the thyroid were excluded because they were still under discussion by the pathologists. The majority of them had moderate toxic symptoms, indicating that the activity of the thyroid was proportionate to the degree of the hyperplasia.

Is hyperplasia of the thyroid more prevalent in the first two decades of life than we have definite knowledge of, perhaps indicating a thyroid activity in response to some demand that cannot be considered far from normal? If so, is this hyperplasia of the thyroid to be sharply distinguished from the hyperplasia associated with Graves' disease, which develops at the average age of 32? I do not believe these questions can be definitely answered at the present time, though there is much evidence suggesting an affirmative answer, at least to the clinical side of the question.

Is the exophthalmos of thyrotoxicosis always associated with hyperplastic goiter? The pathological reports fail to show the presence of hyperplasia in the cases in which exophthalmos was noted by the clinician 6 times in 1909, 4 times in 1910, twice in 1911, and not in a single instance in 1912. In 1912 there were

911 new cases of goiter that came to operation. In most of the exceptions to the rule previous to 1912, we were able definitely to prove that there was an error in noting the presence of exophthalmos.

Should all toxic hyperplastic goiters be included under the term exophthalmic goiter? Possibly there is a small group of cases which should not be included. However, that there is small chance for error in answering this question in the affirmative if we include only those cases coming to operation is indicated by (1) of the cases having diffuse hyperplasia of the thyroid coming under observation from one to three, three to six, six to nine, nine to twelve, twelve to eighteen, eighteen to twenty-four months and over two years from the onset of toxic symptoms respectively, 50, 59, 67, 75, 80, 80, and 87 per cent. had exophthalmos (questionable cases excluded); (2) if we select from any periods in our series 25 consecutive patients having hyperplastic thyroids and mild toxic symptoms, over 50 per cent. have exophthalmos; and if we select from the total number of patients coming to operation during 1911 and 1912 the 25 cases of non-hyperplastic thyroids having the most intense intoxication, exophthalmos is not noted in a single instance. It is quite possible that exophthalmos may be associated with non-hyperplastic toxic goiter, but if so, it is so rare that it must be in a way considered accidental.

Is the symptom-complex accompanying hyperplastic goiter to be directly attributed to disturbed thyroid function? While it has been so considered in this paper only as a matter of convenience for pointing out the association of the clinical and pathological findings, and while I do not wish to enter into a discussion of this subject at the present time, I wish to call attention to a point in support of this theory that, so far as I know, has not hitherto been made, namely, that an individual, aged 22 years, with an adenoma of the thyroid has a definite chance of developing a train of symptoms during the thirty-sixth year so similar to the symptom-complex associated with hyperplastic thyroid that the best-trained diagnosticians are constantly confusing the two conditions.

Can we associate the symptom-complex of non-hyperplastic toxic goiter with any definite pathological change in the thyroid? For the present this question must be answered in the negative.

Correlating the above statistical data, we may safely come to the conclusion that exophthalmic goiter is a definite clinical complex always associated with hyperplasia of the thyroid, and that it should be sharply distinguished from the constitutional state or states that may develop with non-hyperplastic goiter. Still more interesting and convincing is the correlation of a mass of detail with the data given here. This involves too much for a short paper. However, a general conception of the clinical pictures accompanying non-hyperplastic toxic and exophthalmic

goiter is given as an introduction to the paper by Drs. Blackford and Sanford.²

For the purpose of quickly presenting the clinical pictures, let us note the parallelism of thyrotoxicosis and alcoholism and assume that there are three toxic elements in the thyroid secretions, one damaging chiefly the nervous system, one the circulatory system, and the other producing exophthalmos. In exophthalmic goiter all three elements are in excess, but the clinical picture is dominated by a nerve toxin, although in individual cases the circulatory toxin or element producing exophthalmos may seem to be in excess.

The intoxications from non-hyperplastic goiter may be divided into two merging groups: (1) a group in which the cardiac toxin predominates, in which the clinical picture closely resembles and in many instances cannot be differentiated from the cardiovascular complex resulting from alcoholic, luetic, septic, and other well-known toxins; (2) a group more closely approaching the picture of Graves' disease and including the cases that have been erroneously so diagnosed by the mass of the profession.

The average lapse of time between the appearance of non-hyperplastic goiter and toxic symptoms is 14.3 years. That the patient comes under observation three years later indicates that the onset is usually insidious. Nervousness, tremor, loss of strength and weight, as a rule, develop slowly, but may appear suddenly long before definite evidence of myocardial damage. The administration of iodine may cause the sudden appearance of those symptoms with myocardial insufficiency much as they might follow the prolonged drinking bout of an old toper who had not previously shown decided evidence of chronic alcoholism. In some cases the clinical aspect, as noted above, closely approaches that of exophthalmic goiter. However, the symptoms are less complex, less definitely associated, and except for a damaged heart, less intense. There is much evidence to suggest that during the 14.5 years previous to the onset of definite toxic symptoms many of the cases of non-hyperplastic thyroid may be compared to the alcoholic tippler in that if the soil is right they develop arteriosclerosis, in many cases showing the combined picture of thyrotoxicosis and arteriosclerosis.

The development of a typical syndrome of Graves' disease in a case having a definite history of simple goiter means that a hyperplastic goiter has been superimposed upon the simple type.

The onset of exophthalmic goiter is, as a rule, relatively acute and the course of the disease fairly definite. The clinical picture early in the history is that of a toxin acting directly on the more vital organs, more notably the central nervous and vascular systems. Later it is made more complex by the interaction of those organs whose functions have been directly disturbed by the toxin. The order of onset of the most important symptoms based

² A Demonstration of a Depressor Substance in the Serum of the Blood in Exophthalmic Goiter, read before the Association of American Physicians, May, 1913.

on the average of our series is as follows: (1) cerebral stimulation, (2) vasomotor disturbances of the skin, (3) tremor, (4) mental irritability, (5) tachycardia, (6) loss of strength, (7) cardiac insufficiency, (8) exophthalmos, (9) diarrhea, (10) vomiting, (11) mental depression, (12) jaundice, and (13) death.

If the average course of the intoxication be represented by a curve the greatest height is reached during the latter half of the first year, and then suddenly drops to the twelfth month. In many instances it reaches the normal base-line during the next six months. More often it fluctuates with periods of exacerbation for the next 2 to 4 years. Secondary symptoms and exophthalmos may remain, but the active course only rarely continues over 4 years without distinct intermissions. Compare the striking resemblance of the character, order of onset, and course of this train of symptoms with that resulting from the heavy use of alcohol by a susceptible individual over a corresponding period of time. Near the crest of the curve any shock, operation, etc., that treats the patient to another drink may result in tremens or death.

In the average course after the first year the symptoms that may be attributed to long-continued intoxication rather than to a high degree of acute intoxication, *i. e.*, those from the more chronic types of heart, liver, and degeneration of the kidney enter strikingly into the clinical picture. In attempting to construct a composite curve we find that the curves for those symptoms that we can readily attribute to a high degree of immediate intoxication from the thyroid gradually drop while the curves for those findings attributable to a long-continued intoxication of a lower degree gradually rise.

In a later paper I will point out that there is much evidence to suggest that the sudden onset of the toxic symptoms is preceded by a period during which the patient is gradually habituated to the disturbed function of a developing hyperplastic thyroid and that following the disappearance of the clinical manifestations of the intoxication, the patient is still taking care of the products of an overactive gland and if this overactivity with or without clinical manifestations, continues sufficiently long in an individual prone to arterial degeneration, arteriosclerosis with secondary contracted kidneys, high arterial tension, etc., will ultimately develop. The picture of thyreotoxicosis from both hyperplastic and non-hyperplastic goiters may be compared to that from alcoholism in its various degrees and manifestations varying with the dose, length of administration, and susceptibility of the individual.

While the weight of the evidence seems to indicate that, whatever the primary cause, the symptom-complex of exophthalmic goiter is directly attributable to hyperplasia of the thyroid, I wish to repeat that I have so considered it in this paper only as a matter of interest and convenience in associating the pathological and clinical findings.

A DEMONSTRATION OF A DEPRESSOR SUBSTANCE IN THE SERUM OF THE BLOOD OF PATIENTS AFFECTED WITH EXOPHTHALMIC GOITER.¹

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AND

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DURING the past year we have conducted a series of experiments with a view to throwing further light on the relation of the secretion of the thyroid to exophthalmic goiter. We have studied chiefly the cardiovascular effects on the dog of intravenous injections of sterile non-hemolytic blood-serum from nervous individuals and from patients affected with exophthalmic goiter. Also, numerous saline extracts of goiter have been injected intravenously into dogs and the effects on the blood pressure studied.

Gley², in 1911, announced that the serum of certain cases of exophthalmic goiter produces marked cardiac depressor action. He showed, too, that a first injection of potent exophthalmic serum conferred a tolerance of such a nature that subsequent injections of the same serum during the same experiment produced little or no effect.

We have attempted to follow out Gley's researches, injecting intravenously into dogs the serum procured from patients affected with exophthalmic goiter. The effect on blood-pressure was recorded graphically on a long paper kymograph in the usual manner, using the left carotid artery for the arterial cannula. All injections were made into the right femoral vein. The right vagus was exposed and stimulated by induction shock in certain experiments. Blood was obtained by sterile technic from the median basilic veins of the patients, collected in sterile flasks and the serum allowed to separate in the cold. The manifest difficulty that must always be encountered in such work, *i. e.*, the impracticability of obtaining a large supply of blood from each case, has somewhat hindered certain experiments, but we believe that our results are sufficiently interesting to justify reporting.

Gley states that 5 c.c. of serum per kilo dog weight must be used to obtain the best results. We did not have sufficient serum for such large dosage, but obtained excellent results with smaller doses. We have injected $2\frac{1}{2}$ to 4 c.c. serum per kilo dog weight as an average dose, and except when stated to the contrary, this has been the amount of serum.

¹ Read before the Association of American Physicians, Washington, D. C., May, 1913.

² Jour. de Phys. et de Path. Gén., 1911, xiii, 928 to 941; Cleret, *ibid.*, pp. 955 to 970.

We have used for these experiments the sera from twenty-eight patients having exophthalmic goiter. Other sera examined have included those from normal individuals, from patients having goiters without apparent intoxication, and from patients presenting the picture of a long-standing intoxication; presumably due to adenomas of the thyroid. Only the sera from patients with active symptoms of exophthalmic goiter and with markedly hyperplastic glands, as shown by microscopic examination have produced in the dogs injected any definite symptoms of cardiovascular depression.

The curves produced by the sera from patients affected with exophthalmic goiter have naturally fallen into three groups:

Group I. Those sera causing more than 30 mm. of Hg. drop in blood-pressure.

Group II. Those sera causing a drop in blood-pressure, but less than 30 mm. of Hg.

Group III. Those sera causing no appreciable drop in blood-pressure.

The significance of this classification was observed only after an analysis of the individual cases.

Group I. *Six Sera Causing Drops in Blood Pressure of More than 30 mm. of Hg.* The four curves in Chart 1, all of which produced drops in blood-pressure of more than 30 mm. of Hg. when injected in doses of 2.5 c.c. per kilo dog weight, were obtained by injecting sera from patients who were at or near the height of an early and severe intoxication, as shown by the following summaries of the case histories:

CASE 69,123.—Female, aged twenty years. Three months before (March, 1912) noticed suddenly all the typical cardiac, nervous, and muscular symptoms of Graves' disease. Rapid progress during one month to acute vomiting, with great loss of strength. During the third month vomiting ceased, but all other symptoms were marked. (Experiment conducted on dog 253.)

CASE 69,198.—Female, aged fifty years. Slight goiter noted one year before (May, 1911). Definite typical symptoms of exophthalmic goiter began six months before with loss of weight, weakness, and nervousness. Two months before violent crisis, with vomiting, the patient remaining in an acute condition for one week, since then vomiting in spells. In bed most of the time. Loss of thirty pounds in weight in two months. Patient had not noted exophthalmos, which was moderately evident. (Experiment conducted on dog 259.)

CASE 67,993.—Male, aged seventeen years. Three months before (February, 1912) began to lose weight, and all the usual symptoms became evident and rapidly progressed. A month later goiter was noted and the patient forced to bed by weakness. In bed one month, then slight improvement, and has been able to be out of

bed the past month, though a marked intoxication is still present. (Experiment conducted on dog 249.)

CASE 68,628.—Female, aged twenty-three years. Six months before (January, 1912) developed nervous and cardiac symptoms and exophthalmos. She rapidly became worse, and at present shows marked intoxication. Diarrhea for one month. Marked loss of strength and fifteen pounds loss of weight. This patient died in an exacerbation following a single ligation. Unfortunately autopsy on this patient was refused. (Experiment conducted on dog 192.)

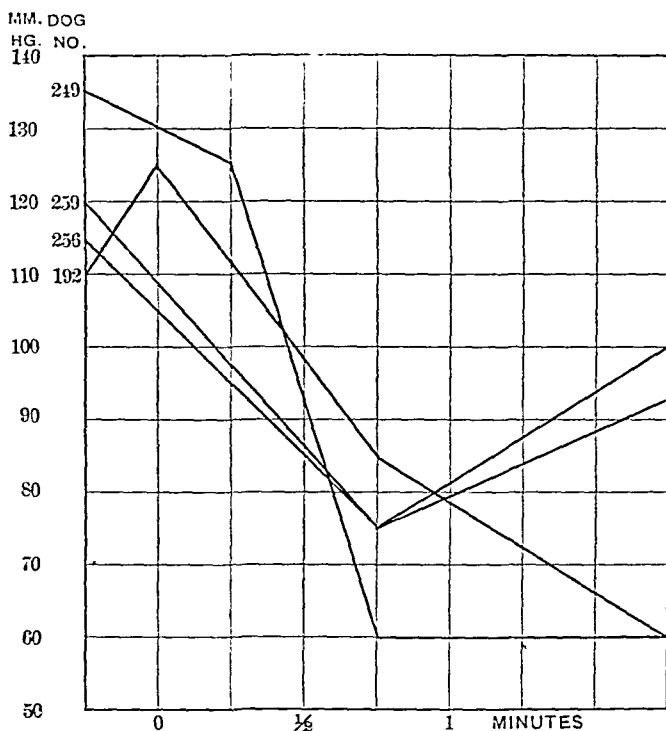


CHART 1.—Drops in blood-pressure of more than 30 mm. after injection of sera from patients in the stage of acute intoxication from exophthalmic goiter.

We believe these histories show conclusively that the four cases were all acute and severe intoxications. Clinical diagnoses in these as well as the following cases have been confirmed by pathological examination of the goiters except the one which terminated fatally.

The two cases shown in Chart 2 are interesting exceptions. One was a fairly acute intoxication of only moderate severity; the other was a chronic intoxication of marked severity. The case histories are as follows:

CASE 75,496. Male, mulatto, aged thirty years. Past history, gonorrhea, syphilis (positive Wassermann), and some alcoholic excess. Two years before (November, 1910) began to lose weight

and strength, and noticed nervous, cardiac, and eye symptoms. Rapid progress to an extreme crisis, with prostration, vomiting, and diarrhea. Then recovery during six months; able to do some work, but still had marked intoxication with a chronic diarrhea.

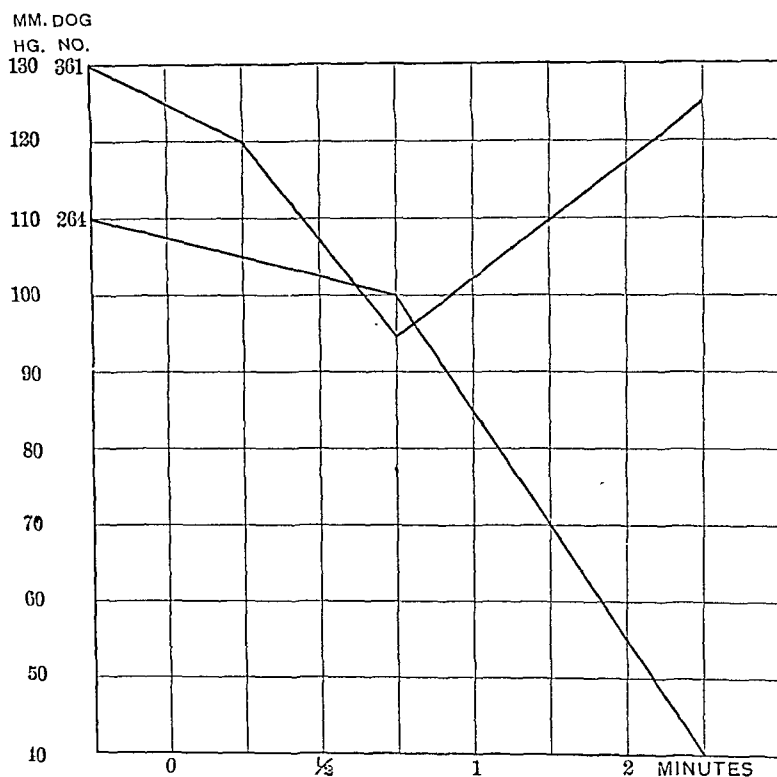


CHART 2.—Drops in blood-pressure of more than 30 mm. after injection of large doses of sera from patients with moderate intoxication from exophthalmic goiter.

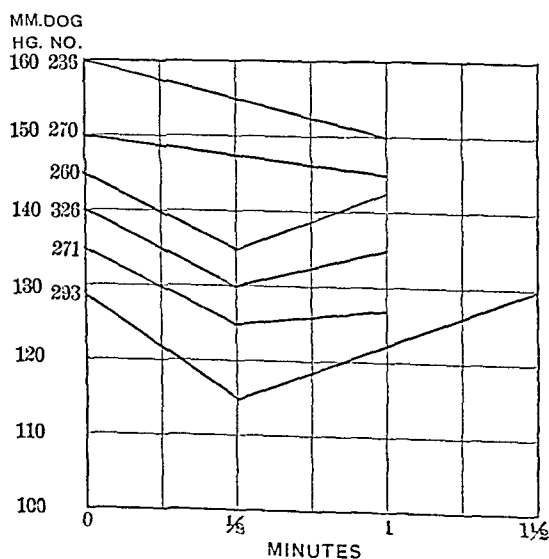


CHART 3.—Drops in blood-pressure of less than 30 mm. after injection of sera from patients not at the height of intoxication from exophthalmic goiter.

Weight forty pounds below normal. (Experiment conducted on dog 361.)

CASE 69,619.—Female, aged nineteen years. Nine months before (October, 1911) had to stop school on account of weakness, dyspnea and nervousness. Symptoms progressively worse until forced to bed six months before. After a rest she improved steadily, and presents a clean-cut but not marked picture of exophthalmic goiter. (Experiment conducted on dog 264.)

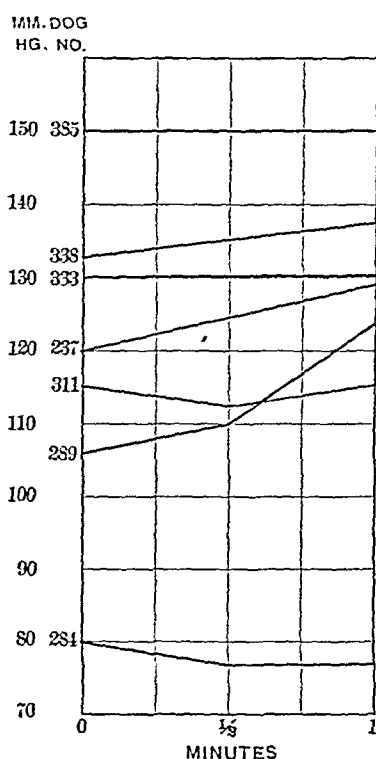


CHART 4.—No effect on blood-pressure following injection of sera from patients with symptoms of intoxication from exophthalmic goiter, but not at or near crisis.

From the two preceding histories we may judge that neither case was extreme. On examining our records we find that the doses of serum given each dog were about three times that used to secure the marked effects shown in Chart 1. Again, we may note that the first case (75,496) was a chronic and severe one, but gave only a 35 mm. drop in blood-pressure, thus almost admitting it into the next group. The second case (69,619) gave a marked fall in blood-pressure, and though not very severe, was not far past a crisis when the blood was taken.

Group II. *Ten Sera Causing Drops in Blood Pressure of Less than 30 mm. of Hg.* Chart 3 shows the curves resulting from injections of six of these sera which caused a fall in blood-pressure of less than 30 mm. of Hg., but which apparently contained a slight amount of the depressor agent. Eight of these ten patients had

been afflicted with the disease for more than a year and none of them seemed near any marked exacerbation. In general it may be stated that these cases were of longer standing and with more pronounced intoxication than those in the following group. Two typical histories from this group are as follows:

CASE 68,883.—Male, aged thirty years. Appendectomy had been done eighteen months before (January, 1910), following which symptoms of exophthalmic goiter promptly appeared and progressed during six months to an extreme intoxication with vomiting, diarrhea, and prostration. Loss of forty pounds in six months. For the past six months steady improvement, and now is nearly normal in weight, though still affected with definite Graves' disease. (Experiment conducted on dog 253.)

CASE 67,283.—Female, aged thirty-six years. Tremor noted for several years. Always more or less nervous. Increased irritability and gradual loss of strength was noted six months before (November, 1911). No dyspnea. Slight diarrhea during the past month. Working steadily to date. (Experiment conducted on dog 236.)

Thirteen Sera Causing no Appreciable Drop in Blood-pressure. Chart 4 shows six curves as typical of the thirteen inert sera which fall into this group. None of the patients seemed to be near a crisis, and eight of them had been sick less than nine months.

These experiments seem to indicate that patients affected with exophthalmic goiter who are suffering from a marked degree of intoxication at or near the height of the clinical curve of the disease (Plummer) possess serum which has a powerful depressor action. The authors have failed to demonstrate this depressor action by similar means in normal sera, or in sera from patients not having markedly hyperplastic thyroids. Also sera from patients with exophthalmic goiter not at or near the crest of the wave of intoxication are less potent or may be entirely inactive.

Since it was not always thought best to bleed very sick patients, only a small number of experiments have been made with sera from patients with severe intoxications. Yet it may be of interest to know that most of the patients that were bled experienced considerable relief from their subjective symptoms after the bleeding.

The results of intravenous injections into dogs of saline extract of ninety goiters of various kinds from human patients have also been made. These experiments may have some bearing on the action of the depressor sera and a brief report of the results is herewith appended.

Intravenous Injections of Saline Extracts. Experiments with extracts of forty-eight exophthalmic thyroids have shown that the markedly hyperplastic goiters considered typical of Graves' disease have a more powerful depressor action than that of the extract of any normal organ examined, including muscle, liver, spleen, pancreas, breast, testicle, thyroid, etc. The fall in blood-pressure

averages 60 mm. of Hg., and is often considerably more, whereas that from other tissues in any comparable dosage is usually less than 25 mm.

Extracts of adenomas of the thyroid, of simple colloid goiters, and of normal thyroids likewise have a depressor action, which, however, has not been found so marked as that produced by extracts of exophthalmic thyroids. Injections equivalent to as much as 5 gm. per kilo dog weight do not cause a fall as great as that of the extracts of exophthalmic goiters in doses of 0.5 gm. per kilo dog weight.

The first injection of any extract of fresh goiter, as of most extracts of tissue, confers a marked degree of tolerance to subsequent injections of the same material during the same experiment.

As is well known, peptone solutions cause a marked fall in blood-pressure on intravenous injection, and subsequent injections show that a tolerance has been established similar to that produced by extracts from goiters. The depressor action of peptone solution is not, however, affected by a previous dose of the extract of exophthalmic goiter, nor is the action of the extract of exophthalmic goiter affected by a previous dose of peptone solution. On the other hand, it is interesting to note that the depressor action of the extract of an exophthalmic goiter is much diminished by a previous dose of potent serum from a case of toxic exophthalmic goiter, and the reverse, judging from a limited number of experiments, is equally true. In other words, a crossed tolerance seems to exist between the depressor action of extract of exophthalmic goiter and of exophthalmic serum. It seems probable, therefore, that the depressor agent in the extract of exophthalmic thyroid and that in the serum from a case of exophthalmic goiter are of the same nature.

No attempt has yet been made to identify the chemical nature of the depressor substances in these extracts of thyroids or of those in sera of patients affected with exophthalmic goiter. From certain experimental evidence it seems that the substance is neither cholin nor ordinary peptone.

CONCLUSIONS. We believe that the work submitted justifies the following conclusions:

Fresh extracts made from exophthalmic thyroids contain a powerful depressor substance.

A powerful depressor substance likewise exists in the sera obtained from certain cases of exophthalmic goiter.

The latter substance is present in direct proportion to the clinical acuteness and severity of the disease.

The sera from patients with non-hyperplastic thyroids do not have a depressor action.

After an active depressor dose of the serum from a case of exophthalmic goiter the depressor action of the extract of an exophthalmic goiter is weakened or abolished. The converse is also true.

ANTITYPHOID VACCINATION.¹

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THE subject of antityphoid vaccination has a great and promising field of usefulness in the United States, both in civil life and in the Army. We shall consider in turn the history of the subject, the methods of preparing the vaccine, its standardization and dosage, the indications for its use, the results already obtained, and its probable value in the future.

The basis upon which the practice of antityphoid vaccination has been built is, of course, the observation that one attack of typhoid fever almost invariably gives permanent immunity against subsequent attacks. Of 2000 cases in the Hamburg General Hospital, only 14 persons were affected twice, and but 1 three times (Dreschfeld). In 500 of Osler's cases in which special inquiry was made as to previous attack, it was found to have occurred in 11, or 2.2 per cent. It is interesting to note that although the immunity usually lasts during life, the immune bodies, nevertheless, disappear from the blood of convalescents within a few months.

The harmlessness of inoculating killed typhoid bacilli into human beings was demonstrated in the year 1896 by Sir A. E. Wright in England and Pfeiffer and Kolle in Germany. The publication of Pfeiffer and Kolle's investigations² antedates Wright's paper by some months. The researches of Pfeiffer and Kolle were conducted on two men, and were remarkably complete and comprehensive, showing, as far as the laboratory methods of that day permitted, the identity of the immunity following an attack of typhoid fever with that produced by the inoculation of killed typhoid bacilli. Thus early was the precedence placed on a solid scientific basis.

Wright's first paper,³ curiously, is entitled "On the Association of Serious Hemorrhages with Conditions of Defective Blood Coagulability," and the inoculation of killed typhoid bacilli was apparently a mere incident in a research upon another subject. The following year, however, he reported on the blood changes in 17 persons, following typhoid inoculation.⁴ It is in this paper that Wright mentions Haffkine's suggestion to him, made a year previously, that the method of vaccination with bacterial cultures, which had

¹ Read before the Harvey Society, New York, February 8, 1913, and published by permission of the Surgeon-General.

² *Deutsch. med. Woch.*, 1896, xxii, 735.

³ *Lancet*, London, September 18, 1896, p. 807.

⁴ Sir A. E. Wright, *British Med. Jour.*, January 30, 1897, p. 16.

been so successfully used in the prophylaxis of cholera, might, *mutatis mutandis*, be applied to the prevention of typhoid fever. Wright appears to have been convinced by his series of 17 cases that the prevention of typhoid fever by vaccination was a possibility. He suggested at this time (1897), its use in armies and among the personnel of hospitals. This really constitutes the beginning of the present vaccination campaign against typhoid fever. Wright continued his work with enthusiasm, and in 1898, while serving on the Plague Commission in India, vaccinated about 4000 men of the British Indian Army, with excellent results.⁵ Soon after his return to England, in 1897, there occurred an extensive outbreak of typhoid fever at the Barming Asylum, Maidstone; and as he himself was unable to go he sent, first, Sir David Semple and afterward Sir William B. Leishman to conduct inoculations on about one hundred of the attendants. There also the results were highly gratifying, since no cases occurred among the inoculated.

Soon afterward, in 1900, came the Boer War, and antityphoid inoculation, having already given such a good account of itself, upon Wright's recommendation its use was authorized by the War Office among the troops destined for South Africa.

The vaccination was voluntary, and, as a matter of fact, is still voluntary in every country except in the United States. Some men were inoculated before leaving England, others on the transport during the long voyage to South Africa, and in a few instances in the field after arrival. For this purpose Wright and Leishman furnished some 400,000 doses, but it is believed that only 100,000 men received one or more.

No complete statistics of antityphoid vaccination in South Africa have ever been published, and they probably do not exist. We know in general that there were 57,684 cases of typhoid and 8022 deaths among 380,605 men.⁶ This gives a morbidity rate of 151.56 per 1000, a result which does not differ markedly from our own rates in the Spanish-American War, where no vaccination was in force. In our service a larger number of cases were diagnosticated, but the death-rate was, nevertheless, much less than in South Africa.

TABLE I.

	Total strength.	Cases.	Ratio per 1000.	Deaths.	Ratio per 1000.
English Army, Boer War, 1900 to 1903	380,605	57,684	151.56	8022	21.08
American Army, Spanish War . . .	107,973	20,738	192.6	1580	14.62
Wright's statistics, Boer War . . .	19,069	226	11.84	39	2.04

Wright collected statistics covering the inoculation of 19,069 soldiers.⁷ Among this number there were 226 cases of typhoid

⁵ Wright, *Lancet*, London, September 6, 1902, p. 654.

⁶ Leishman, *Antityphoid Vaccination*, *Glasgow Med. Jour.*, 1912, lxxvii, 408.

⁷ McCrae, in *Osler's Modern Medicine*, 1909, ii, and Wright, *Lancet*, London, September 6, 1902, p. 654.

fever and 29 deaths, while among 150,231 unvaccinated soldiers, there were 3739 cases of typhoid fever, as appears in the following table:

TABLE II.—Boer War, English Troops, Wright's Statistics.

	Number	Cases.	Ratio per 1000.	Deaths.	Ratio per 1000.
Vaccinated	19,069	226	11.84	39	2.04
Unvaccinated	150,231	3739	24.88	?	?

At Ladysmith,⁸ the following results were obtained:

		Morbidity.	Mortality.
Vaccinated	1,705	35 cases (2.05 per cent.)	8 deaths (0.47 per cent.)
Unvaccinated	10,529	1,489 cases (14.14 per cent.)	329 deaths (3.13 per cent.)

At Modder River⁹ there occurred 26 cases among 2335 vaccinated (11.1 per cent.) and 257 cases among 10,981 unvaccinated (23.4 per cent.).

Wright considers that the incidence of the disease was diminished about one-half and the mortality even more. His conclusions, however, were based upon incomplete statistics, and were not accepted at the time by his colleagues in the service. The frightful death-roll remained in spite of explanations. It appeared to have been impossible during the war to keep accurate records or even to vaccinate systematically, and consequently the whole question was left in considerable confusion. This was made worse by the receipt of many unfavorable reports: some asserting that the vaccine did no good, others maintaining that it actually increased the number of cases and deaths.¹⁰ Before the end of the war, as a result of this unfavorable attitude, the British War Office suspended the practice of inoculation and appointed a commission to reinvestigate the whole question. Fortunately this commission, under the chairmanship of Dr. C. J. Martin, of the Lister Institute, included in its membership Sir William B. Leishman, to whom fell the experimental part of the proposed investigation. He conducted extensive experiments at Aldershot in regard to dosage and the changes in the blood serum following inoculation. More recently additional studies have come from his laboratories at the Royal Army Medical College, and the importance of this work of Leishman's can scarcely be overestimated, and although he made only a few changes in Wright's vaccine, they were important ones.

The commission in their statistical studies and experimental work at Aldershot obtained evidences of a considerable degree of protection, and their interim report, rendered in 1904, was decidedly favorable. It introduced accurate and practical methods of obtain-

⁸ Report of Committee on Antityphoid Vaccination, Bull. de l'Acad. de Méd. de Paris, January 24, 1911.

⁹ Ibid.

¹⁰ A. Crombie, Lancet, London, 1902, i, 1201, and 1902, ii, 436.

ing reports from twenty-four regiments, totaling almost 20,000 men, and, as the results have shown, the work was successful in rehabilitating an almost discredited procedure. As a result, inoculations were resumed in certain selected regiments, to which a medical officer, especially trained in typhoid diagnosis, was permanently attached. By this means, in a comparatively short time, accurate records were obtained. As many volunteers as possible were vaccinated before the regiments left England for India, and efforts to obtain additional volunteers were continued at the Indian stations until the greater number of the men were vaccinated, many regiments having as many as 90 to 100 per cent. protected.

AMERICAN EXPERIENCE. For some years we had followed the work of Wright and Leishman with interest, and Wright's visit to this country in 1907 added to our knowledge of his work with vaccines, although at that time Wright was more interested in vaccine therapy in general than in typhoid prophylaxis. We, however, as military sanitarians, always with the possibility of a war confronting us, were more taken with Wright's former advocacy of antityphoid vaccination than with his newer, brilliant theories and discoveries.

The necessity for some means of preventing, or at least controlling, typhoid fever in military camps, in addition to sanitary measures, was a continual spur, driving us on to investigate everything which offered any hope of success. It was, therefore, with great interest that we followed the results obtained by Colonel Leishman¹¹ among troops of the Indian Army.

In 1909 Leishman published the first comprehensive report of the results of vaccination in certain selected Indian regiments (see accompanying table).

The experience of the 17th Lancers, which had been brought to our attention by Colonel Leishman early in 1908, was so striking that we felt much encouraged about the possibility of having at last an effective prophylactic, and so began to take an active interest in the vaccine. The writer had been stationed at the Army Medical School only a few months when the late Surgeon-General Robert M. O'Reilly directed him to make preparations to try out the method on our own troops.

As the quickest and best way of beginning, orders were issued in June, 1908, for him to proceed to London, where he could learn from Colonel Leishman and his assistants, at the Royal Army Medical College, their method of preparing the improved vaccine. There he was given the run of the laboratory and was given every facility for learning their methods, including a transfer of the culture (Rawlings) used in preparing the vaccine.

¹¹ Journal Royal Army Medical Corps, London, 1907, viii, 463, and 1909, xii, 166.

TABLE III.—Showing the Results of Antityphoid Inoculation in Sixteen Units of the British Army, up to June 1, 1908.

Unit.	Medical Officer.	Station.	Total strength (actual).	Inoculated.			Non-inoculated.		
				Number.	Cases.	Deaths.	Number.	Cases.	Deaths.
2d Royal Fusiliers	Capt. A. B. Smallman	Trimulgherry	1,013	196	10	1	815	59	9
17th Lancers	Capt. E. J. Luxmore	Meerut	616	322	3	0	294	71	12
Brigade, R. A.	Capt. E. G. Lithgow	Pindi (from Transvaal)	370	60	0	0	310	7	0
14th Hussars	Lieut. C. E. Fawcett	Bagnalore	647	386	2	0	261	4	1
2d Dorsets	Lieut. E. G. Anthonisz	Wellington	1,107	199	1	0	908	6	0
3d Coldstream Guards	Lieut. J. H. Graham	Cairo	705	569	1	0	136	13	1
2d Leicesters	Lieut. H. S. Sherren	Belgaum	963	346	3	1	617	17	1
1st Connaught Rangers	Lieut. A. D. O'Carrol	Dagshai (from Malta)	483	300	0	0	183	2	1
3d Worcesters	Lieut. W. H. Forsyth	Wynberg	900	220	0	0	680	3	0
1st Dragoon Guards	Lieut. G. H. Stevenson	Umballa	592	450	0	0	142	0	0
1st Yorks	Lieut. de C. O'Grady	Cairo	893	470	0	0	423	0	0
1st Suffolks	Lieut. J. B. G. Mulligan	Malta	900	400	0	0	500	0	0
3d Royal Rifles	Lieut. R. W. D. Leslie	Crete	879	190	0	0	689	0	0
2d Bedfords	Lieut. C. M. Drew	Gibraltar	700	320	0	0	380	3	1
Brigade, R. A.	Lieut. A. S. Littlejohns	Pretoria	375	247	1	0	128	2	0
1st Lan. Fusiliers	Lieut. F. D. G. Howell	Chakrata	940	796	0	0	144	0	0
		Totals	12,083	5473	21	2	6610	187	26

CASE-INCIDENCE PER 1000.

	Inoculated.	Non-inoculated.
Among the whole of the above sixteen units	3.8	28.3
Among the "exposed" units, that is, in which cases of enteric had occurred	6.6	39.5
"Exposed" units, less Royal Fusiliers (the unit inoculated with the "old vaccine")	3.7	32.8

SUMMARY. There are only 4 cases among the above 21 which had received two doses of the new vaccine; all recovered; 3 of the 4 had been noted as extremely mild, and the diagnosis of enteric in one of these was doubtful.

Later (1908) a trip was made to Berlin, where at the Institute for Infectious Diseases he learned of the German experience with typhoid prophylactics. The complete report of the German investigations, published in 1905, is accessible, and will be passed over quickly.¹²

The occasion for the German investigation was the excessive prevalence of typhoid fever among the colonial troops in southwest Africa. All attempts to control the epidemic by the usual sanitary methods having been unsuccessful, recourse was had to vaccination. The Institute for Infectious Diseases was intrusted with the task of investigating the vaccines already proposed, the selection of some reliable method, and the preparation of the vaccine, should one be decided upon.

Comparative tests were made of vaccines prepared according to the methods of Pfeiffer and Kolle, Wright, Neisser-Shiga, Wassermann, and Bassenge-Rimpau by the staff of the Institute,

¹² Veroffent. a. d. Gebeit. des Militar-Sanitatswesens, Berlin, 1905, Heft 28.

consisting at that time of Professors Kock, Kirchner, Gaffky, Doenitz, Kolle, and Wassermann.

Small groups of men were immunized with each vaccine and the blood-serum subsequently tested for bacteriolytic amboceptors by Pfeiffer's test and for agglutinins by the usual technique. Although the bacteriolysins and agglutinins did not run parallel, they found that the Pfeiffer-Kolle vaccine gave a much greater degree of protection than any other, and it was therefore adopted. They objected to Wright's vaccine because of his use of broth cultures, since it is well known that bacterial contaminations are difficult to avoid or to detect in fluid media.

The Pfeiffer and Kolle vaccine consisted of a salt-solution suspension of fresh agar cultures of typhoid of such a strength that 1 c.c. contained two normal loopfuls, or 4 mg. of fresh bacterial substance. The bacteria were killed by heating the flasks, from one and a half to two hours, in an incubator regulated for 60° C. After tests for sterility, 10 per cent. of a $\frac{1}{20}$ solution of phenol was added. The dose used at first was one, two, and three loopfuls of killed culture contained in 0.5, 1.0, and 1.5 c.c. of vaccine; as this dosage, however, produced severe general and local reactions, it was subsequently reduced to 0.4, 0.8, and 1 c.c. The interval between doses was ten days; the site of inoculation was the breast at the level of the second rib.

This vaccine was used in the German Colonial Army, which consisted at that time of about 16,500 men, of whom 7287, or less than one-half, volunteered for the inoculation. Among this number there were 1277 cases of typhoid,¹³ and a study of their distribution shows clearly the undeniable advantages of prophylactic inoculation, even though the results were not nearly so good as have since been obtained in India and in our own country. The weak point of the German vaccine lay, apparently, in the high temperature at which it was killed and in the excessive dosage.

One may briefly and roughly summarize their results by saying that there was a reduction among the vaccinated of one-half in the number of cases, a much higher percentage of light attacks, 50 to 36, and a much lower percentage of fatal cases, 6.4 to 12.8. If we distinguish between those receiving one, two, and three doses we find that the percentage of fatal cases was 60, 33, and 8 respectively. This is in agreement with later experience in showing that little protection is to be expected from one dose. Among the uninoculated there was 1 death in every 7.8 cases, while among those receiving three doses there was not only a lower morbidity but only 1 death in every 36 cases.

Kuhn¹⁴ concluded that the immunity was largely lost after one

¹³ Shoemaker, Herero Campaign, International Clinics, Philadelphia, 1909, 19th s., ii.

¹⁴ Ibid.

year, since after that time there was little difference between the sick- and death-rates of the vaccinated and unvaccinated.

Colonel Firth, R. A. M. C.,¹⁵ reasoning from similar data, found that the vaccines in use today in India maintain a high degree of protection for at least two and a half years.

The history of antityphoid vaccination can be divided into two stages. The first period includes the early experimental work of Pfeiffer, Kolle, Wright, and Wright's immunization of 4000 men of the British Indian Army, the Boer War and the German campaign against the Hereros. The most accomplished during this period was the reduction of the morbidity to about one-half among the vaccinated and a rather greater diminution of the case mortality.

EXPLANATION OF EARLY FAILURES. Disappointment at the poor showing made by antityphoid vaccination during this first period was widespread, and for a time prevented any serious consideration of its further use. The loss of interest was due to two things: (1) The undoubted failure to secure anything like absolute protection against infection and death, and (2) what was perhaps even more important, Wright's unfortunate doctrine of a negative phase. To consider, first, the failure to secure a high degree of protection, we now know from the writings of Colonel Leishman,¹⁶ that much of the vaccine sent to South Africa, was, from our present point of view, overheated in its preparation or otherwise rendered inert. Later investigations by Colonel Leishman, Majors Harrison, Grattan, and others have shown that overheated vaccines are almost worthless. Poor and incomplete immunity, due to faulty vaccines, is therefore a preventable condition, and this source of error once known, its avoidance and the regular production of efficient, powerful vaccines is a simple matter.

WRIGHT'S DOCTRINE OF THE NEGATIVE PHASE. The other cause of disappointment and lack of interest was the doctrine of the negative phase. The doctrine that vaccination could actually and materially increase one's susceptibility to infection for a time was generally believed, and was advocated by none more emphatically than by Wright himself. It mattered not that experience with other vaccines had shown no increase of susceptibility beyond the normal. Wright built up the theory of a dangerous negative phase upon questionable determinations of the opsonic index and upon certain phenomena observed in the production of diphtheria and tetanus antitoxin in animals. It is well known that the antitoxin content of the blood of the animals used will fall from a previously high level after each administration of toxin. The conditions, however, are not at all comparable: in human beings

¹⁵ Journal Royal Army Medical Corps, 1911, xvi, 589.

¹⁶ Harben Lecture, Antityphoid Vaccination, Journal Royal Institute Public Health, London, July, August, and September, 1910.

no such enormous doses are used, and further, in the beginning of the immunization of a horse, when the doses are small and widely spaced, it is doubtful if there be any reduction of resistance below the normal level. Upon such theoretical grounds, and upon isolated instance of severe typhoid fever following immediately after vaccination, was this doctrine built up, and, very curiously, it was uncritically accepted by the greater part of the medical world. Wright even went so far as to discover a condition of increased susceptibility to smallpox immediately following vaccinia. However, vaccination against smallpox in the presence of an epidemic was too firmly rooted to be successfully questioned. The doctrine of the negative phase in practical immunization appeared only in relation to typhoid fever; nothing was heard of it at that time in connection with bubonic plague and cholera, except from Wright.

In an article published by him in 1902,¹⁷ on the results of vaccination in South Africa, the following is found: "In bringing this summary to a conclusion, I am anxious to reëmphasize a point already emphasized by me in previous papers: that there is, in connection with all protective inoculations, a risk to be considered. There is the risk that (1) in the case where the patient's resistance is naturally low, or has been reduced, as is often the case, by a previous attack of typhoid fever; (2) in the case where the patient is inoculated with a full dose of vaccine in actually infected surroundings; (3) in the case where the patient is inoculated with an excessive dose, or is reinoculated too soon, the system may be left more open to infection at a period when it stands in need of protection. The facts seem to me to indicate the reality of this risk."

In a hasty search through the later publications of Wright few definite statements can be found to justify his former attitude. In later papers he speaks quite guardedly, observing that the risk of a negative phase comes seriously into consideration only when excessive doses of vaccine are employed, or when the prophylactic inoculations are undertaken in the actual presence of infection."¹⁸

He adds that the remedy lies near at hand, and consists of a reduction in the size of the dose.

In the preface to his book on *Studies on Immunization*, published in 1909, he no longer insists on the dangers of increased susceptibility, but speaks of the practicability of controlling the negative phase and of immunizing a patient without risk or appreciable delay. He even goes farther and approves the therapeutic use of anti-typhoid vaccine, a position which would have been absurd if vaccination lowered the patient's resistance to typhoid toxins.

¹⁷ Lancet, London, September 6, 1902, p. 654.

¹⁸ Wright's *Studies on Immunization*, London, 1909, and Boston Med. and Surg. Jour., May 9, 1903.

The best discussion of the subject from the opposite point of view we owe to R. Pfeiffer,¹⁹ who questioned Wright's data, based as it was principally upon the opsonic index. Pfeiffer and Friedberger convinced themselves that guinea-pigs inoculated with large doses of vaccine did not show any increased susceptibility to intraperitoneal infection with living cultures, but, on the contrary, their resistance was distinctly increased, and that this change was apparent within a few hours. This increase of resistance continued to be present up to the time when the formation of specific antibodies began. These results are in agreement with the earlier work of Pfeiffer and Isaef²⁰ on non-specific resistance as contrasted with specific immunity.

What can be said on the practical side of the question? Is it true in actual practice that vaccination increases susceptibility to infection? A definite and conclusive negative answer can be made to these questions. Leishman²¹ relates his experience in inoculating one hundred attendants at the Barming Asylum, Maidstone. There, if ever, evidences of increased susceptibility would have been present. The inoculations were made, at the height of the epidemic, with doses of vaccine considerably larger than are now used. Yet no single case occurred, and Leishman was convinced that the dangers of a negative phase were more theoretical than real.

Cullinan²² in 1901 vaccinated 500 persons at the Richmond Asylum, Dublin, during an epidemic lasting five months; among these only 1.36 per cent. contracted the disease, and almost all were in the incubation stage when inoculated; on the other hand, of the 114 uninoculated nurses, 14.9 per cent. became infected.

More recently, Spooner²³ in Boston, and Hachtel and Stoner in²⁴ Baltimore have immunized the personnel of the Boston and Baltimore hospitals. This is, of course, equivalent to vaccinating in the presence of an epidemic, yet they detected no indication of increased susceptibility immediately following vaccination.

Spooner²⁵ has recently used vaccine, during an epidemic, with satisfactory results. He writes as follows: "The water-supply of a limited number of people in a small Vermont village became contaminated with the typhoid organism from the excreta of an isolated individual who had died from the disease six months prior to the epidemic. The original primary cases, 17 in number, appeared simultaneously. Within a week 29 of the remaining 48 who had been exposed to the disease through the water-supply had been

¹⁹ *Centralbl. f. Bakteriöl.*, 1908, 1 Abt., Referate, xl, 712.

²⁰ *Zeitschr. f. Hyg. u. Infektionskrankh.* Leipzig, 1894, xvii, 355.

²¹ Harben Lecture, September, 1910.

²² H. M. Cullinan, *Antityphoid Vaccination during an Epidemic in Dublin*, reported by Wright, *British Med. Jour.*, October 26, 1901, p. 1226.

²³ *Jour. Amer. Med. Assoc.*, 1912, lix, 1359.

²⁴ *Trans. Assoc. Amer. Phys.*, 1912, xxvii, 343.

²⁵ *Ibid.*, 1364.

inoculated; 19 remained uninoculated. Among the latter, 5 cases developed; among the former, 1. This case presented his first symptoms immediately following the first dose of vaccine, and the disease ran a mild course."

The immunization of those in the immediate neighborhood of typhoid fever patients brings up this question in acute form. We have, so far as possible, immunized all contacts and have seen only good results. Many, however, still hesitate to practice in typhoid fever what is regularly done in the case of variola.

Peterson²⁶ relates the following: "An interesting fact, which in my mind removes any doubt of its efficacy, was that in one house there were fourteen occupants, seven of whom were in the acute stage of typhoid. The remaining were immunized with no further development of typhoid in the house. The house and surroundings were about as unsanitary as any I ever saw or expect to see."

As we look back upon this dark period we can see that the unfortunate doctrine of a harmful negative phase arose in part, at least, from a false interpretation of the relative failure of vaccination in South Africa. That failure we now believe was due not to any false or dangerous element in the principals of prophylactic vaccination, but to the use in improper dosage of an overheated and comparatively inert vaccine, which simply failed to give the desired protection.

Leishman and his co-workers discovered the fault and found the remedy. They reduced the amount of heat used in killing the cultures and also diminished the dose. At Aldershot they tried out various doses upon human beings and adopted that now used in practically all countries, 500,000,000 and 1,000,000,000 bacilli, as this quantity was sufficient to produce an abundance of immune bodies and rarely caused severe reactions.

The doctrine of a negative phase was so simple, so reasonable, and, if true, so important for everyone to know that it came early to the knowledge of all reading physicians. Backed as it was by abundant statistics from South Africa it was accepted as true by almost everyone, and its overthrow has not yet been fully accomplished. In England and in India little of it is now heard; in this country, in the army and in the naval service, its conquest dates back only three years. In civil life we still hear it referred to by men who have not yet used antityphoid vaccine. Owing to this doctrine, there is in France, both in the Academy of Medicine and in the army, an active and energetic opposition to the use of vaccination in the military and naval services.

The writer's personal experience with antityphoid prophylaxis began, as previously stated, in 1908, when he was ordered abroad by the War Department to study the subject at first hand. In

²⁶ J. J. Peterson, Control of Typhoid Fever by Vaccination, Southern Med. Jour., 1912, v. 257.

Colonel Leishman's laboratory, in London, he found that vaccine was prepared by growing in broth a single selected strain (Rawlings) of the typhoid bacillus. The flasks used were long, flat bottles which were incubated lying on their sides, giving a thin layer of medium in contact with the air. The bottles of broth, after preliminary incubation to determine their sterility, were inoculated with a pipette from a broth culture. After twenty-four to forty-eight hours' incubation the growth was usually sufficiently heavy to require the addition of a small quantity of plain broth to reduce the bacterial count to the quantity desired, 1,000,000,000 to the cubic centimeter. The counting was done by an ingenious wet method devised by Harrison, using washed red blood-cells from a definite quantity of blood with which to compare the number of bacteria in an equal quantity of emulsion. The vaccine was killed by heating for one hour at 53°C. , and after cooling 0.4 per cent. of lysol was added as a matter of safety.

The English vaccine is, therefore, a killed broth culture made from a single strain of the bacillus, which was originally selected because it emulsified well from agar slants. Preliminary trials of this organism showed that it agglutinated well in immune serum, and produced in good quantities all measurable kinds of antibodies in animals and man. This strain is still in use in England and in our military service, and although we have searched from time to time for a strain with greater antigenic properties, none has yet been found.

In Germany the only prophylactic used at all extensively was made according to the method of Pfeiffer and Kolle. Aside from their use of agar media the characteristic of the vaccine is its standardization by the loop method, a normal loop being one which holds 2 mg. of fresh bacterial substance. Experience has shown that a single slant would furnish about ten normal loopfuls and that the quantity of vaccine obtained per test-tube was 5 c.c. This enables one to compare the dosage with that used by the English and ourselves, since we obtain from 15 to 20 c.c. of prophylactic per tube. The German dosage was, therefore, about three or four times as great. Their method of killing and the temperature used are also important for a complete understanding of their vaccine. They also used a single strain of the bacillus, the culture known as 151 being selected from a large number because of its exceptional binding properties. Wassermann particularly has insisted that the property of binding and of producing antibodies is of more importance in the selection of an organism for the production of vaccine than its virulence.

Our own vaccine is made from a single strain of bacillus (Rawlings), and the culture is grown on agar in flasks for eighteen hours. At first, when small quantities only were needed, test-tubes were used, but as the quantities increased Kolle flasks were substituted, each with an agar surface equivalent to twelve tubes.

The culture used is plated out—a dozen colonies are fished on to double sugar-tubes,²⁷ and from these macroscopic agglutinations are made. Any culture which fails to develop the characteristic appearance on double sugar, or to give a good agglutination, is discarded; from the remaining cultures agar slants are inoculated and the next day emulsified in a small quantity of broth; with this thick emulsion the Kolle flasks are inoculated by means of a large swab. If they show no contamination after eighteen hours' incubation the growth is washed off in a small quantity of salt solution, and, while a sample is being counted, the thick suspension is heated in large flasks in a water-bath for one hour at 53° to 54° C.

The killed vaccine is diluted with large quantities of salt solution until the desired concentration, 1,000,000,000 to the cubic centimeter, is obtained. Finally 0.25 per cent. of trikresol is added as a matter of safety. After aërobic, anaërobic, and animal tests have been made the vaccine is put up for shipment in hermetically sealed ampuls of normal glass.

The aërobic and anaërobic tests for sterility are made with large quantities of vaccine, several cubic centimeters to each tube and plate; the animal tests consist in the inoculation of a mouse and guinea-pig, with 0.5 and 1.5 c.c. for the exclusion of tetanus spores, and a rabbit with three doses at ten-day intervals to determine the immunizing power of the vaccine. The average titer of the agglutinating rabbit serum obtained with the last eighteen batches of vaccine after thirty days was 1 to 18,000.

Morphological tests of purity, using Gram's stain, are made at each stage of preparation, and a few lots of vaccine have been discarded because of contamination with the *Bacillus subtilis* group, but none have ever been rejected because of the animal tests. They are continued, however, because of the occurrence of a number of deaths from tetanus in India after the administration of plague vaccine. In one case a batch was discarded because it failed to produce blood agglutinations in the rabbit test.

We have used agar cultures because of the ease of detecting contamination and to avoid the injection of extraneous materials contained in fluid media.

The vaccine is killed by heat rather than chemicals, using the least amount possible to obtain sterility, and it is protected against subsequent contamination by trikresol.

Our vaccine is essentially the whole body of the *Bacillus typhosus*, changed as little as possible in killing, suspended in a convenient quantity of salt solution. Such a vaccine has the merit of simplicity, is readily and easily prepared, and is constant in quality.

What then have been the results obtained with it in protecting human beings?

²⁷ F. F. Russell, Jour. Med. Research, Boston, 1911, xxv, 217.

We began to use the prophylactic early in 1909, after first submitting the project to a board of officers selected from among the distinguished members of the medical reserve corps of the army, since it was realized from the start that little could be accomplished without the support of the medical profession of the country. This board recommended the introduction of voluntary vaccination, and work began in earnest early in 1909.

All who had seriously studied the subject of bacterial vaccines and typhoid immunity, realized that the use of prophylactic inoculation was theoretically possible and justifiable, but few considered it practical. For the army, however, the question was too important to be slighted, and a repetition of the experiences of the Spanish-American War must be prevented in one way or another.

Antityphoid vaccination was taken up with a firm conviction as to its value, but with many misgivings as to our power to convince others, or to secure sufficient volunteers to give it a fair trial. It is difficult to overcome the inertia of great bodies like the army, and there is always the danger of ignorant and malicious criticism.

The first doses given to the laboratory staff seemed to have a greater importance, and the operation was more momentous than the occasional therapeutic use of other vaccines, since so much depended upon an auspicious beginning.

When the immunization of the laboratory force had been completed, available volunteers seemed for a time to have been exhausted; but the news spread, and practically all of the medical officers in and about Washington volunteered, and, in turn, sent their wives and children, friends and servants. This helped us over the first obstacle, and we began to obtain volunteers from the hospital corps. By the end of 1909, 1887 persons had received the prophylactic treatment, and during the next year (1910) 16,073 additional volunteered. During the first part of 1911 volunteers continued to present themselves in increasing numbers, so that immunized men came to be present in practically every garrison in the United States proper. The measure was no longer strange to the medical corps, nor to the enlisted personnel of the army. We noticed, however, as with all voluntary measures, that there was great inequality in different garrisons, depending, of course, on the interest and enthusiasm or opposition of the commanding officer and the surgeon. Such conditions are inseparable from voluntary measures. In the department of the East, where the measure was actively pushed by the chief surgeon, Colonel John Van R. Hoff, more volunteers were obtained than in all other departments together. Lectures and missionary work among the officers were resorted to, as we early saw the truth of the well-known fact that the men follow cheerfully wherever the officers lead.

One commander²⁸ finding typhoid present in his garrison and epidemic in the neighborhood, succeeded in having the entire regiment vaccinated by refusing permission to leave the limits of the military post to anyone not protected against typhoid by vaccination or attack of the disease.

It is understood that in India volunteering was encouraged by refusing the opportunity, so dear to the soldier, of active service, to regiments whose quota of inoculated was small. Such incidents merely show the difficulty of protecting the health of a community which refuses to accept or to interest itself in measures for its own welfare.

In the English service, vaccination against typhoid has always been, and still remains, a voluntary measure; but we in March, 1911, introduced unequivocal compulsion on the occasion of the mobilization of a maneuver division in Texas.

In the army the duty of the physician is, of course, as in civil life, to treat the sick and minister to the wounded in the best and most approved manner; but the military surgeon has, beside, another duty, more important by far than the humanitarian one referred to: the duty of preserving the health of all under his charge and of having at all times the maximum number of able-bodied men on the firing line and of keeping them healthy enough to remain there. With this duty clearly before us, compulsory vaccination against typhoid was recommended for every person in the division not already protected by an authenticated attack of typhoid or by recent vaccination.

At this time we had already obtained records of vaccinations of approximately 20,000 persons, and knew that the preparation we were using was harmless; we knew too that it caused few severe reactions in healthy persons, and that no vaccination, however severe the immediate reaction may have been, had been followed by permanent injury to the individual; and further, that by all possible laboratory tests the immunity conferred was identical with and equal to that remaining after typhoid fever. Statistics of typhoid among vaccinated and unvaccinated troops were beginning to confirm, on a large scale, the laboratory tests.

It was impracticable from the data at hand to give accurate statistics comparing the rate among the vaccinated with the unvaccinated, but enough had been learned for our purpose. It was necessary to protect that body of 20,000 men against typhoid as well as against smallpox and other infectious diseases. We were convinced that this could best be done if every man not already protected were vaccinated, and a recommendation to this effect from Surgeon-General George H. Torney was approved by the War Department, and vaccination was ordered on March 9, 1911, for all troops on the border.

²⁸ Lyster, *Military Surgeon*, 1911, xxviii, 528.

There is an apparent basis for objection to compulsory vaccination in typhoid fever, based on the reasons for universal vaccination against smallpox. In smallpox susceptibility is universal, and no other measure of sanitation or protection gives immunity. It is vaccination or nothing. With typhoid fever, under ordinary conditions, the problems presented are decidedly different. Not everyone is susceptible. During the Spanish-American War Reed, Vaughan, and Shakespeare²⁹ showed that one-fourth to one-third of those exposed contracted the disease.

Susceptibility to infection is, therefore, much less than with smallpox. Further, there are other good and practicable methods of prevention: pure water, good sewerage, and supervision of milk and other food supplies, properly carried out over a long series of years, will cause this disease to practically disappear, as it has in many parts of England and Prussia. This is well known, and is a condition we are looking forward to in our own country. Improved sanitation in the large cities is constantly reducing the typhoid death-rate, and under such circumstances neither compulsory nor voluntary vaccination need be considered. The conditions with which we have to deal in actual or mimic warfare are so entirely different that one can scarcely recognize the highly contagious disease which absolutely paralyzes regiments, divisions, and armies as of the same nature as the sporadic typhoid of cities. We cannot forget that typhoid fever is proteus-like in the variety of its disguises.

The following table shows the havoc wrought in some modern wars:

TABLE IV.

	Strength.	Typhoid cases.	Typhoid deaths.	Killed in action or died of wounds.	Died of disease.	Wounded.	Missing.
Franco-German War,							
German Army	73,393	6965	28,269	15,240	68,498	12,854
Spanish-American War,							
American Army . .	107,973	20,738	1580	243	2,565	1,445
Boer War, British Army	380,605	57,684	8022	7,702	13,250	22,829
Russo-Japanese War,							
Russian Army	17,033	34,000	9,300	141,800

We can all remember the experience of 1898 in military camps; it is well to review a few of the points brought out so clearly by Reed, Vaughan, and Shakespeare³⁰ lest we forget the lessons of experience. They found that typhoid fever appeared in over 90 per cent. of volunteer regiments within eight weeks of going into camp, and in some regiments of regular troops it appeared

²⁹ Abstract of Report on the Origin and Spread of Typhoid Fever in United States Military Camps during the Spanish-American War of 1898, Washington, Government Printing Office, 1900, p. 191.

³⁰ Ibid.

in three to five weeks; it also appeared both in small and large encampments in the Northern as well as in the Southern States. They stated their belief that "with typhoid fever as widely disseminated as it is in this country the chances are that if a regiment of 1300 men should be assembled in any section and kept in a camp the sanitary conditions of which were perfect, one or more cases of typhoid would develop."

They observe that typhoid fever is more likely to become epidemic in camps than in civil life because of the greater difficulty of disposing of the excretions of the human body. A man infected with typhoid fever may scatter the infection in every latrine in his camp before the disease is recognized in himself.

They demonstrated that water was not an important cause of the spread of the disease and that flies undoubtedly served as carriers of the infection; that the spread was through contact and was characterized by a series of company epidemics, each having more or less perfectly its own individual characteristics.

They showed that an organization once infected continued to produce new cases, even though it changed its camp site or travelled long distances by land or by sea. This doctrine, radical at the time, has since been made simple through the discovery of temporary and chronic bacillus carriers.

In this war the mortality from typhoid fever was 86.24 per cent. of the total. The morbidity was 192.65 per thousand of mean strength, or a little less than one-fifth. The mortality per thousand of mean strength was 14.63.

When orders were suddenly issued early in 1911 for the mobilization in Texas, California, and along the Mexican frontier of the largest body of troops in the field since the Spanish War, the question of typhoid prophylaxis ceased to be academic and became a practical question insistent on solution. The mobilization plans did not provide for fixed camps, where water supplies and even sewerage systems might have been arranged, but called for active service in the field, under conditions simulating, as closely as possible, actual warfare. Indeed, we did not know but that a campaign into Mexico might not follow quickly the assembling of the troops. Even the incinerators recently used in maneuver camps for the destruction of excreta by fire were forbidden, as being too heavy and cumbersome and too expensive to form part of the equipment of moving troops.

Experience during the Spanish-American War had taught what to expect in large and protracted camps. In eight weeks it was thought that through the agency of flies, dust, and the inevitable close contact of crowded camps and more crowded tents there would be some cases of typhoid, and that probably the advances in field sanitation could be relied upon to protect against a repetition of that war's disasters. Although conditions could not have been

expected to have been as bad as in 1898, there would likely have been typhoid fever enough to have handicapped some portion of our small force had an advance across the border become necessary.

With these possibilities in view and with complete confidence in both the effectiveness and harmlessness of antityphoid vaccination, it can be understood why, in the opinion of the Surgeon-General, compulsory vaccination was to be preferred to the half-way measure of volunteering.

The results fully justified the position taken. The maneuver division, as it was called, was ordered to mobilize in Texas, California, and along the Mexican border in March, 1911. They remained in camp and on the border patrol for a period of four months, when the greater number were returned to their garrisons. A few thousand men had already received the prophylactic, and the others were vaccinated as rapidly as they arrived. The vaccine was prepared at the laboratory of the Army Medical School in Washington and shipped as rapidly as it could be used. During the thirty days after the receipt of orders, approximately 60,000 doses were prepared and delivered. As the full course of three doses occupies twenty days we had no great difficulty in supplying the vaccine as rapidly as it was needed.

In addition to the main divisional camp at San Antonio, smaller camps occupied by separate brigades were established at Galveston, Texas, and San Diego, California. At Galveston there were about 4500 persons, and at San Diego, 3000. No cases of typhoid were reported among the troops in Galveston, although the chief surgeon estimated that there were 192 cases among the civil population of the city during the period of the encampment. From San Diego only 2 cases³¹ were reported, and 1 of these was doubtful. Other detachments, smaller in size, were scattered along the border, yet there was no typhoid. The camp in San Antonio was the largest and best known of the maneuver camps, and the interest of the public has centred upon it. For a period of four months, beginning in March, 1911, almost 13,000 troops were located there, and anyone who visited it knows that all the elements which tend to affect the health of men under canvas were controlled better than they had ever been before. The sanitary difficulties of camp life arise mainly from the lack of established water, sewer, and scavenger systems, and these difficulties were overcome at San Antonio by new and ingenious, yet practical, expedients. Flies, the cause of so much trouble in 1898, were kept down to a minimum by a series of simple yet effective company crematories. In drawing a mental picture of a military camp, one is quite apt to overlook the necessary camp animals. At San Antonio, for instance, there were 6000 horses and mules scattered here and there in close proximity

³¹ Annual Report of Surgeon-General of United States Army, 1912, p. 51.

imity to the quarters of the men, and the proper disposal of the stable refuse by fire was in itself no small undertaking.

One can best judge of the combined effects of vaccination and sanitation by comparing this camp with the one located at Jacksonville in 1898.³²

TABLE V.

1898, *Spanish-American War, Camp at Jacksonville, Florida.*

Number of troops	Cases of typhoid certain.	Certain and probable.	Deaths from typhoid.	All deaths
10,759	1,729	2,693	248	281

1911, *Camp at San Antonio, Texas.*

12,801	2	11
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At Jacksonville there were assembled 10,759 men, among whom there were 1729 undoubted cases of typhoid, and including those in which a diagnosis of typhoid was probable there were 2673 cases, with 248 deaths. This camp lasted approximately as long as the camp at San Antonio in 1911; both camps were situated in about the same latitude, and each had artesian well water of excellent quality, yet in 1898 there were over 2500 cases of typhoid fever, with 248 deaths, and in 1911 only 2 cases, with no fatalities.³³ We know that the immunity was not due to lack of exposure, since there were reported to the health office 49 cases of typhoid fever, with 19 deaths, among the civil population of the city of San Antonio during the period of encampment.

Our men were not rigidly confined to camp, but had leisure and opportunity to visit the neighboring cities of San Antonio and Galveston. Thousands of soldiers spent more or less time in these cities, where they ate, drank, and slept; in fact, became for the time being a part of the community. In Galveston especially, where a ten-minute ride carried one from camp to the heart of the city, the number of men visiting town was large. The soldier is not overparticular where he obtains food and drink: restaurants, good and bad, lunch wagons, street-corner stands, all have his patronage. Fruits and pastry and sweets were purchased of hucksters lined up along the camp boundaries. The best kind of camp sanitation alone could not have prevented typhoid in the presence of all these possible chances of infection, with the disease as prevalent as it was in the adjoining cities. What it did do was to reduce the number of chances of infection and prevent the appearance of secondary cases from the two which actually occurred.

³² Kean, Jour. Amer. Med. Assoc., 1911, lvii, 713.

³³ Annual Report of Surgeon-General of United States Army, 112, p. 51.

Many other striking illustrations of the efficacy of vaccination might be instanced; one, however, must suffice.³⁴ A cavalry regiment of about seven hundred men engaged in a twenty-one-day practice march through a part of Tennessee, where typhoid fever is endemic throughout the year. During their march of six hundred miles there was no attempt to boil or sterilize the drinking water. The amount of sickness was practically *nil*, and no cases of typhoid developed. Following a previous practice march in the same region ten cases occurred, and the further spread of the disease at that time was finally stopped by wholesale vaccination.

Compulsory vaccination in the Southern maneuver camps was ordered on March 9, 1911; the next step, June 9, 1911, was the extension of the order to all recruits; since which time 2000 to 3000 recruits have received the prophylactic treatment each month, at the same time being vaccinated against smallpox. If the vaccinia be severe the second dose of the typhoid prophylactic is postponed a few days, but in no other way has it been necessary to deviate from this routine of simultaneous vaccination against the two diseases. The two vaccinations are completed by the time the man has been twenty days in the service. It is our present practice to revaccinate against both smallpox and typhoid at the beginning of each four-year period of enlistment. This is not because the immunity has by that time disappeared, for its duration is not yet known. It no doubt diminishes gradually, as in the case of smallpox, yet in the service it is desirable to maintain the army in a maximum state of protection against infection at all times, and it does not seem advisable to omit vaccination until an outbreak of typhoid shows the disappearance of all immunity. Smallpox has been almost entirely suppressed; there were only 5 cases among American troops in 1911, with no fatalities, and typhoid has ceased to be the scourge of former days.

The next and most important step was the extension of compulsory prophylaxis to all persons in the service under forty-five years of age; this was ordered September 30, 1911. In the United States proper the order was not fully executed before January 1, 1912. In the Philippines it was not carried out until the first part of 1913.

If vaccination gives the protection we believe, its good effect should show in the total number of cases reported in the army year by year, and the following table and charts have been arranged to show these facts:

³⁴ Lyster, Military Surgeon, 1911, xxviii, 528.

TABLE VIII.—Typhoid Fever (United States), among Enlisted American Troops.

Year.	Mean strength.	Absolute cases.	Number deaths.	To each 1000 soldiers of the command the ratios are:	
				For cases.	For deaths.
1901	26,515	250	17	9.43	.64
1902	39,736	341	34	8.58	.86
1903	42,264	246	12	5.82	.28
1904	43,940	247	12	5.62	.27
1905	42,834	153	13	3.57	.30
1906	40,621	230	12	5.66	.28
1907	35,132	124	7	3.53	.19
1908	46,316	136	11	2.94	.23
1909	57,124	173	16	3.03	.28
1910	55,680	129	9	2.32	.16
1911	55,240	44	6	0.80	.11
1912	58,119	15	2	0.26	.03

NOTE.—This includes all information available in the Surgeon-General's Office to April 1, 1913. Strength for officers and enlisted men for 1912 is only approximate, as it was not possible to obtain a true strength on that date.

TABLE IX.—Showing the Number and Proportion of Typhoid Fever Cases Contracted before Enlistment and among the Protected (United States Proper only) Officers and Enlisted Men.

Year.	Total cases.	Total deaths.	Infected prior to enlistment.	Among the vaccinated.	
				Number of cases.	Number of deaths.
1909	173	16	?	1	0
1910	129	9	?	4	0
1911	44	6	?	7	0
1912	18	3	5	6	0

TABLE X.—Typhoid Fever, 1901 to 1912, for the Whole Army, Officers and Enlisted Men, at Home and Abroad.

Year.	Mean strength.	Cases.		Deaths.		Percentage of total cases.	Occurring among those who were vaccinated.	
		No.	Ratio per 1000 of mean strength.	No.	Ratio per 1000 of mean strength.		Cases.	Deaths.
1901	81,885	552	6.74	74	.88	13.0		
1902	80,778	565	6.74	69	.85	12.2		
1903	67,643	348	5.14	30	.44	8.6		
1904	67,311	293	4.35	23	.33	7.8		
1905	65,688	206	3.14	20	.30	9.7		
1906	65,159	373	5.72	18	.27	4.8		
1907	62,523	237	3.79	19	.30	8.0		
1908	74,692	239	3.20	24	.31	10.0		
1909	84,077	282	3.35	22	.26	7.8	1	0
1910	81,434	198	2.43	14	.17	7.1	7	0
1911	82,802	70	.85	8	.10	11.4	11	1
1912	88,478	27	.31	4	.044	14.8	8	0

From these figures and charts the deductions would seem quite clear. They are based upon accurate observations of from 70,000 to 80,000 men each year, and are as accurate as only great care can make them. We see a sudden drop in both morbidity and mortality

during the last two years, which corresponds with the increase in the use of a prophylactic immunization during the same period.

During the year 1913 there have been no cases of typhoid fever reported up to October 1, and in order to compare it with previous years the following table has been prepared, which shows the total number of cases for the last six years, for the first three-quarters of each year. From this it is apparent that the beneficial effects of vaccination are much greater than previous experience would lead one to believe.

TABLE XI.—Typhoid Fever. United States Officers and Enlisted Men, United States Army.

	Year.	Jan.	Feb.	Mar.	Apr.	May.	June.	July.	Aug.	Sept.	Oct.	Nov.	Dec.	Total for 9 mos.
Voluntary	1908	5	6	4	2	3	11	14	31	25	26	12	8	101
	1909	4	10	6	4	11	15	26	14	16	45	20	6	106
	1910	8	11	1	4	2	6	12	27	21	16	20	11	92
	1911	3	3	3	7	4	4	4	7	4	4	1	0	39
Compulsory	1912	1	2	2	0	0	3	1	3	1	4	0	1	13
	1913	0	0	0	0	0	0	0	0	0				0

Paratyphoid fever included in figures for 1908, but excluded in other years.

Cases paratyphoid: 1909, 3; 1910, 3; 1911, 2; 1912, 3; 1913, 0.

Since the Spanish-American War, medical officers of the army have given much attention to the prevention of this disease, and have greatly reduced the frequency of its occurrence. The greatest care, however, in sanitation and hygiene did not appear to be successful in reducing the number of cases much below 150 per annum in the United States for the present strength of the army, or an average number of not quite 3 cases to every 1000 men.

The importance, for statistical purposes, of the year 1912 arises, as may be noted, from the fact that not until then were there complete statistics for a calendar year, covering compulsory immunization of the entire army. All previous tables were based upon either voluntary immunization of small numbers or mixed voluntary and compulsory immunization, and such tables were always open to the objection that volunteers constitute a group of thoughtful, careful men, who would naturally be less liable to infection than the rank and file of the army. This objection is disposed of by the compulsory use of typhoid prophylactic, and the year 1912 demonstrates fully what may be accomplished when the measure is used fearlessly and regularly upon a large number of persons.

In the navy³⁵ "the compulsory use of typhoid prophylactic was inaugurated on January 1, 1912, and the inoculation of practically the entire naval personnel has been completed without a single serious result or casualty. Only a small fraction of 1 per cent. had reactions necessitating rest in bed, and but a small percentage of individuals required to be excused from duty. As this policy has

³⁵ Annual Report of Surgeon-General of United States Navy, 1912, p. 16.

been put into effect so recently, it is impracticable to formulate any comparative data relative to the rate of the disease, but reports, made in response to a bureau circular letter; show that in men who had received the three injections only one authentic case of typhoid fever has occurred, although three were reported as such in which laboratory findings failed to verify the diagnosis. One mild case occurred in a man who had but two inoculations. One officer, known to be a typhoid carrier, was found to be free of the typhoid bacillus subsequent to receiving the three injections required. The prophylactic administered to the personnel on the Asiatic station was prepared at the Naval Hospital, Canacao, Philippine Islands."

All other antityphoid vaccine used by the navy was prepared in our laboratories at the Army Medical School.

The following table shows the amounts of vaccine furnished from the Army Medical School for the use of the army, navy, militia, and others.

TABLE XII.

Year.	Army.	Navy.	Militia.	Others.	Total.
1909	6,000 c.c.	1,000 c.c.	7,000 c.c.
1910	68,592 c.c.	7,251 c.c.	75,843 c.c.
1911	237,540 c.c.	50,000 c.c.	22,241 c.c.	6,692 c.c.	316,473 c.c.
1912	147,463 c.c.	187,284 c.c.	28,751 c.c.	11,218 c.c.	374,716 c.c.
	<hr/> 495,595 c.c.	<hr/> 237,284 c.c.	<hr/> 50,992 c.c.	<hr/> 26,161 c.c.	<hr/> 774,032 c.c.

ESSENTIALS FOR A TYPHOID VACCINE. The essential requirements for a prophylactic vaccine are that the immunization shall be harmless, that the process shall not be attended with unpleasant symptoms, and that the immunity shall be reasonably long.

In addition, the vaccine to be of real service must be available in ample quantity at short notice, which means, of course, that the vaccine must either be stable enough to withstand long storage or that the method of preparation be so simple that unlimited quantities will be available on short notice for use in epidemics and among troops upon mobilization.

That the immunization is harmless is sufficiently clear, since about 200,000 men, as nearly as can be estimated, have already been immunized with our vaccine without a single fatality or serious complication.

At San Antonio 1 case of musculospiral neuritis was apparently directly due to the vaccination. Our directions distinctly call for a subcutaneous inoculation, as slow rather than rapid absorption is desired; yet some physicians persist in giving deep hypodermics, as was evidently done in this case.

At Guantanamo, Cuba, in 1911, 1 case occurred which has aroused some comment.³⁶ A private of the marine corps received

³⁶ United States Naval Bulletin, 1911, v. 336. Freeman, Southern Med. Jour., 1912, v. 4.

one dose of vaccine. He felt perfectly well at the time and previous to the inoculation. Two days later he was admitted to the hospital, acutely ill with high fever (104.6°), headache, and dulled intellect. Within twenty-four hours after admission he began to grow rapidly worse. He died seventy-six hours after admission and seven days after vaccination. The autopsy record and examination of the ileum, preserved at the Naval Medical School, show clearly that the man at the time of his death was at the end of the second or beginning of the third week of the disease. His infection was, therefore, at least a week old when the single dose of vaccine was given. Whether or not it affected his condition it is impossible to say. Certainly, one is not justified in drawing any inference as to the harmful effects of vaccination from a single case, and that an ambulatory one, since walking cases are notorious for the late intensity of symptoms and high mortality.

It is not unusual to read in public prints of fatalities following vaccinia, and a recent instance, reported by Broeckerhoff,³⁷ is quite comparable to the Guantanamo case. A nine-year-old boy was vaccinated against smallpox on May 7; at the time he fainted and was sent home in the company of some other boys. On arrival he was pale, and complained of pains and headache, and went to bed immediately. The physician who saw him reported the vomiting of blood and the presence of dark blood in the stools. There was no appreciable rise of temperature, and the pulse was small and rapid. There was no morbid change at the site of vaccination. On May 9 he died, without developing any new symptoms. The autopsy showed definitely that the cause of death was hemorrhage from typhoid ulcers, and that the vaccinia was in no way responsible for his death.

In this connection it is necessary to remember that we never administer the prophylactic to any but the healthy. If there be any doubt about possible illness the treatment is postponed until a diagnosis can be made.

We also know that, except in rare instances, the immunization is not attended with unpleasant symptoms. When the practice was first introduced, careful records of all general reactions were kept, and the following table shows the rarity of severe general reactions; in over 97 per cent. of persons the general reaction was mild or absent.

TABLE XIII.—Showing Degree of Severity of General Reactions.

Dose.	Number of doses.	Per cent. absent.	Per cent. mild.	Per cent. moderate.	Per cent. severe.
First dose	45,680	68.2	28.9	2.4	0.3
Second dose	44,321	71.3	25.7	2.6	0.2
Third dose	38,902	78.0	20.3	1.5	0.1
	128,903				

³⁷ Centralblatt f. Bakteriologie, 1912, 1 Abt. Ref., iv, 549.

Severe reactions occurred in only one to three persons per thousand, and the experience of the navy using our vaccine is confirmatory of our own.

The degree of immunity is, of course, not absolute, since 27 cases (including 8 so far reported for 1912), with 1 death from hemorrhage, have been reported during the past four years.

In the light of our experience with vaccinia it is improbable that we shall ever obtain an immunization process which will give absolute immunity. There is an individual variation among persons just as among animals. In the laboratory it is not unusual to find certain animals refractory to immunization, and we cannot expect more uniformity among human beings.

The army is as well protected against smallpox as repeated vaccination can make it, yet we had in the entire army, American and native troops, 21 cases in 1908, 7 in 1909, 17 in 1910, and 20 in 1911, a total of 65 cases, with 2 deaths in four years, against 27 cases of typhoid fever, with 1 death, after antityphoid vaccination in an equal length of time.

The duration of the immunity following our method of prophylaxis has not yet been determined. The interval between vaccination and the onset of typhoid fever in the 27 cases referred to is as follows:

TABLE XIV.

Case.	Date.	Patient.	Interval.	Station.
1	Aug. 2, 1909	R. J.	6 days after 2d dose	Transport
2	Mar. 6, 1910	A. T.	9 months after 2d dose	Philippine Islands
3	June 7, 1910	A. S.	1 month after 3d dose	Fort Mott, N. J.
4	July 24, 1910	R. J. S.	4½ months after 3d dose	Philippine Islands
5	Aug. 5, 1910	E. L.	3½ months after 3d dose	Fort Benj. Harrison, Ind.
6	Aug. 5, 1910	B. F. H.	1 month after 3d dose	Fort Washington, Md.
7	Aug. 7, 1910	S. P.	2 month after 3d dose	Fort Washington, Md.
8	Dec. 20, 1910	H. D. C.	4 months after 3d dose	Philippine Islands
9	Jan. 12, 1911	J. B.	9 months after 3d dose	?
10	May 12, 1911	R. K.	5 days after 3d dose	Point Loma, Cal. ³³
11	May 9, 1911	J. D.	21 days after 3d dose	San Antonio, Texas
12	June 12, 1911	R. C. K.	Point Loma, Cal.
13	July 10, 1911	G. M.	San Antonio, Texas
14	Sept. 25, 1911	F. H. S.	3 months after 3d dose	Fort Sam Houston, Texas
15	Oct. 13, 1911	H. K. M.	6½ months after 2d dose	Fort Sam Houston, Texas
16	Oct. 13, 1911	E. W.	Fort Sam Houston, Texas
17	June 1, 1911	A. P. B.	7 months after 3d dose	Japan
18	Nov. 26, 1911	F. J. T.	20 months after 3d dose	Philippine Islands
19	Dec. 28, 1911	J. C.	6 months after 3d dose	Porto Rico
20	Jan. 28, 1912	W. C. E.	21 days after 3d dose	Fort Slocum, N. Y.
21	June 4, 1912	J. G. K.	4 months after 3d dose	Field, Cal.
22	Aug. 3, 1912	H. S. D.	12 months after 3d dose	Fort Williams, Me.
23	Aug. 30, 1912	W. McC.	17 months after 3d dose	Fort Oglethorpe, Ga.
24	Oct. 15, 1912	A. E. S.	21 months after 3d dose	Fort Leavenworth, Kan.
25	Oct. 18, 1912	A. J. B.	13 months after 3d dose	Washington, D. C.
26	April 15, 1912	F. F.	4 months after 3d dose	Schofield Barracks, H. T.
27	Aug. 16, 1912	M. C. (P. S.)	8½ months after 3d dose	Philippine Islands

³³ History of Typhoid in 1905.

In only 4 instances in the 27 reported cases was the interval between vaccination and infection less than one month; should anyone feel inclined to interpret these infections as instances of a negative phase, they would also serve to illustrate its rarity.

Within three months after vaccination there were 8 cases.

Within six months and over three months there were 6 cases.

Within twelve months and over six months there were 6 cases.

Within eighteen months and over twelve months there were 2 cases.

Within twenty-four months and over eighteen months there were 2 cases.

Interval unknown, 3 cases.

It is evidently impossible from this small collection of cases occurring in the military service to draw any conclusions as to the duration of the immunity.

The experience of the English Army in India shows³⁹ that the immunity begins to fall after two and a half years. This, however, does not assist us greatly, since the difference in the preparation of the vaccine and our use of three doses to the English two leads us to hope for a greater degree and longer duration of the immunity. That there is some justification for this expectation can be shown by comparing the results obtained among English troops in India in 1911⁴⁰ with those obtained in the entire American Army at home and abroad for the same year.

TABLE XV.—Typhoid Fever, 1911.

	Total strength.	Absolute numbers.		In vaccinated persons.	
		Cases.	Deaths.	Cases.	Deaths.
English troops in India . . .	72,371	170	22	106	11
Entire American Army . . .	82,802	70	8	11	1

RATIOS.			
	Admissions per 1000.	Deaths per 1000.	Case mortality.
India	2.3	0.3	12.9 per cent.
United States and colonies	0.85	0.1	11.4 per cent.

In considering this table one should, of course, remember that typhoid is a much more common disease in India than in either the United States or its colonies, and the chances of infection are therefore greater. Vaccination has also been used in India since 1904, and it is possible that the interval between vaccination and infection may in some cases have been a long one. It is probable, nevertheless, that our agar vaccine and the use of three doses rather than two are the main factors in producing better results in our service.

³⁹ Firth, Jour. Royal Army Med. Corps, 1911, xvi, 589.

⁴⁰ Report of Health of Army for 1911, London, 1912, liii, 37.

The old idea that the protective power of the vaccine lasted only so long as agglutinins and other antibodies were demonstrable in the serum has been largely discredited, since we know that agglutinins, at least, are present in the serum of vaccinated persons generally as long as they are demonstrable in persons who have had typhoid, and who are, as a rule, immune for life.

Further essentials of a good vaccine are that it be available in ample quantity at short notice; that it be stable enough to be stored for at least three months, and to be shipped about the country for use by any physician. These requirements rule out the greater number of the vaccines proposed. It is possible, in fact probable, that the future will give us better vaccines than we now use, yet no vaccine can be seriously considered which does not fulfil these conditions.

The principal modifications suggested in late years are those of Vincent, of the French Army, and Metchnikoff and Besredka.

Vincent's⁴¹ vaccine is made as follows: several strains isolated in the neighborhood in which the vaccine is to be used are grown on agar twenty-four to forty-eight hours; the growth is taken up in salt solution and kept at 37° C. from two to four days; after centrifugation the supernatant fluid is sterilized by being shaken with ether, which is then allowed to evaporate. Three or four injections are given at short intervals.

Vincent reports the following results from Algeria:

2632 not vaccinated	171 cases	64 per 1000
129 vaccine of Wright	1 case	7 per 1000
81 vaccine bacillary polyvalent	0 cases	0 per 1000
73 autolysate polyvalent	0 cases	0 per 1000

These and other results so far reported by Vincent are excellent, and, thanks to his work, opposition is rapidly disappearing in France, and vaccination is now being used to some extent in the army and navy. We have had no personal experience with it.

Metchnikoff and Besredka⁴² have conducted the most extensive investigation of recent years, using chimpanzees as test animals. They found that in these animals killed vaccines were powerless to prevent typhoid fever when overwhelming doses of infectious material were used, but that prophylactic immunization with sensitized living bacilli gave them power to resist even large doses, such as may occur in milk-borne epidemics. Interesting and valuable as this work of Metchnikoff and Besredka undoubtedly is, it nevertheless deals with a limited number of apes, and for practical purposes cannot, in the opinion of the writer, be compared to the work in the military service with nearly 200,000 human beings.

⁴¹ Compt. Rend. de l'Acad. Sci., February 7 and 21, 1910; Compt. Rend. de la Soc. de Biol., July 29, 1911; Bull. de l'Acad. de Méd., 1910, xl, 226; Ibid., 1911, iv, 63.

⁴² Ann. de l'Inst. Pasteur, 1911, xxv, 193.

It is evident from Tables VIII and X and Charts I and II that our present vaccine is conferring immunity in as great a degree as has ever been done by any vaccine. It is certain that in the military service, typhoid prophylaxis is quite as successful as vaccination against small-pox, our old ideal of what a prophylactic measure

ADMISSION RATES FOR TYPHOID FEVER,
UNITED STATES (ENLISTED MEN)

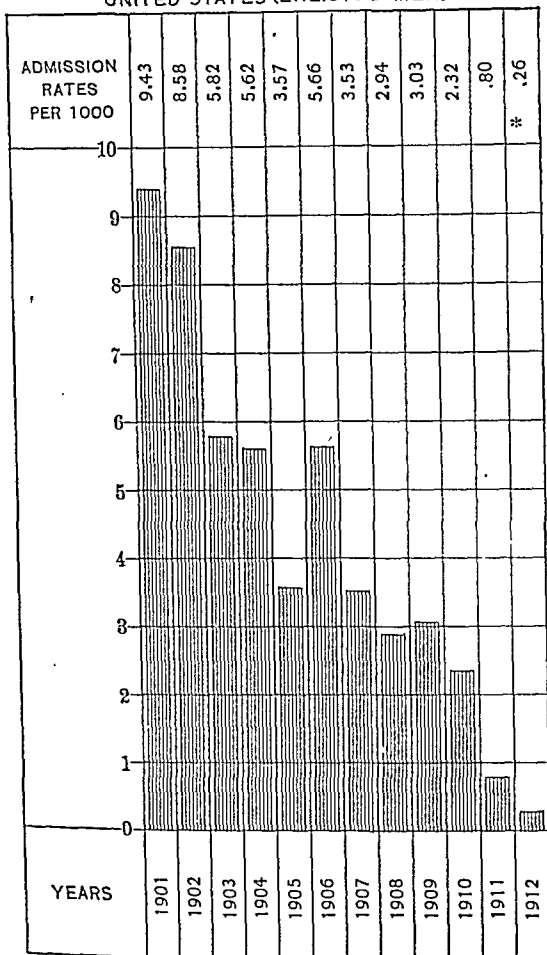


CHART 1.

DEATH RATES FOR TYPHOID FEVER,
UNITED STATES (ENLISTED MEN)

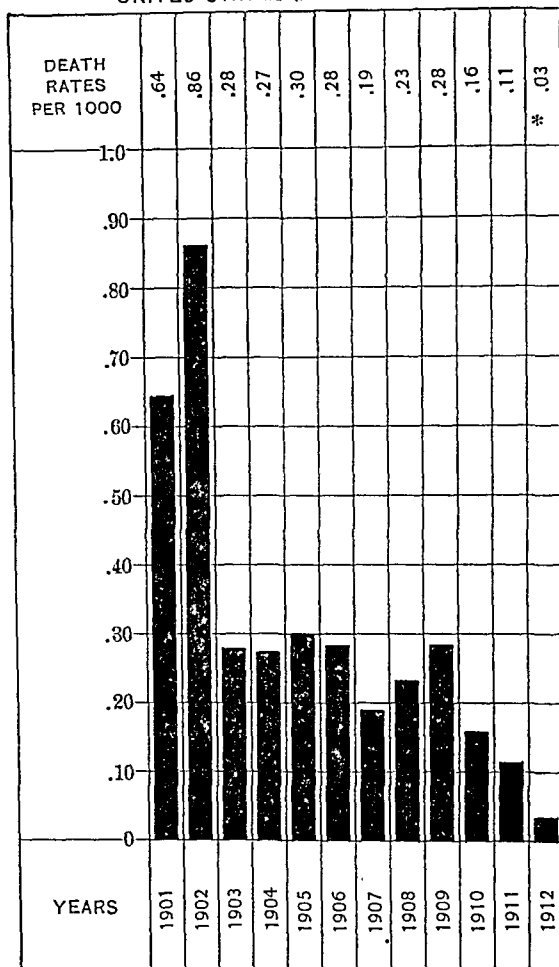


CHART 2.

* All information available in the Surgeon-General's Office January 10, 1913. Later reports may show additional cases. Strength only approximate, as it was not possible to obtain a true strength on January 10, 1913. Antityphoid vaccination, begun voluntarily in 1909, was made compulsory in 1911.

should accomplish. It is evident from this that the opinion held by many scientists that living vaccines and viruses are superior to dead vaccines, and that a high degree of immunity can only be conferred by the use of living vaccines, must be reconsidered at least so far as typhoid fever and smallpox are concerned; our experience has definitely demonstrated that the immunity conferred by dead typhoid bacilli is in no way inferior to the immunity against smallpox conferred by living vaccine virus.

Excellent as the living, sensitized vaccine of Metchnikoff undoubtedly is, there are at the present time certain insuperable objections to its use in our service; it consists of living bacteria, and is not stable and cannot be stored even for short periods. Although it appears to be safe to inject attenuated vaccines subcutaneously, it is still a question whether they could be handled safely and might not accidentally infect persons by the mouth. Another objection is the possibility of contamination. This is not theoretical, as it has occurred twice in the history of cholera vaccination, with disastrous effects upon the progress of the movement. Contamination of a killed vaccine can be absolutely ruled out at the time of its preparation, and enough antiseptic can be added without damage, to prevent further accidental contamination. Living vaccines can never be made and handled with the same confidence, and this circumstance remains a serious objection to the use of such vaccines on a large scale.

There is another point of equal if not greater importance. We in the army and navy have come to rely upon universal compulsory vaccination. Does anyone imagine that the time is ripe for any physician to recommend, or for cabinet members to order, every man in the service to submit to vaccination with living typhoid bacilli? From conversations with persons in authority the idea has been firmly impressed upon the writer that the time for that has not yet arrived.

Would it be possible to achieve the same good results by voluntary vaccination with a living vaccine of equal protective power? How many would volunteer for vaccination under such circumstances? Certainly no more than at present. In the English Army in India, after eight years of success and hard work, 85 per cent. of the men are vaccinated, and it seems improbable that this percentage can be appreciably increased. We have learned by experience that typhoid searches out and often finds the unvaccinated man: 12 out of 18 cases in 1912 and 37 out of 44 in 1911 were among the uninoculated portion of our army. It seems, therefore, probable that greater good will be accomplished by the compulsory use of an admittedly safe vaccine than by the voluntary use of a living prophylactic.

Our experience since 1909 has left no doubt about the success of antityphoid vaccination in the army and navy. The measure has come to stay. Is it not, however, desirable under other circumstances as well? On certain points there is a pretty general agreement. Most physicians believe that the personnel of hospitals and dispensaries should be protected, since experience has shown an unduly high rate among internes, nurses, and attendants. Hachtel and Stoner⁴³ state that in six Baltimore hospitals the

⁴³ Amer. Jour. Public Health, ii, 157.

incidence among nurses and attendants over a period of five years was twelve to twenty times greater than the rate for the city. Joslin and Overlander⁴⁴ found the rate among nurses in Boston was 161 per 10,000 of population as compared with twenty for the State of Massachusetts, or eight times as high.

We should, however, go a little farther than this and vaccinate all who in any way come in contact with the sick, including the family and servants in contact with typhoid fever cases.

There are many other groups of persons to be vaccinated about which there is no dispute, such as those who live in industrial villages, mining towns, and isolated and temporary asylums, and especially schools.

In lumber camps, the camps of engineers, contractors, and pleasure-seekers the use of the typhoid prophylactic will richly repay the time and trouble necessary for its administration.

Its use, however, is not limited to these classes of persons. The typhoid death-rates for New York, Boston, Chicago, and most other large cities in the North are low, ranging from 4.7 in Bridgeport to 17.5 in Philadelphia in 1910, and so long as the inhabitants of these cities remain at home they run little danger of contracting the disease. Remaining at home, however, is a thing most of us are not accustomed to do; we send our patients and our families, and go ourselves to the country, seaside, and mountains, where the typhoid-rate may be many times as high as at home. Such terms as vacation typhoid and travel typhoid are common expressions, and show the danger to which we are constantly exposed. A technical term of importance in this connection is residual typhoid, that is, the typhoid which remains in a community after pure water and good sewerage have been introduced. This is the typhoid we have been fighting in army posts the past few years; it is the typhoid which remains in New York, Washington, and Richmond after these cities have been furnished with pure water. It is due to many factors: milk, flies, contaminated foods, contact with chronic and temporary carriers, and with typhoid cases. Shall nothing be done to reduce the typhoid fever which remains after pure sanitation has done its best? We know from army experience that vaccination will reduce it surely and without danger.

Leaving the subject of residual typhoid in sanitary areas, let us consider the chances of infection in unsanitary regions, either urban or country. Here we know the chances of infection are much greater; we all know how common typhoid is in this country every summer and autumn. Osler says (*Principles and Practice of Medicine*): "From 1900 to 1909 the death-rate in the registration areas was 29.5 per 100,000. It is estimated that from 35,000 to 40,000 persons die from typhoid fever every year, so that at a moderate

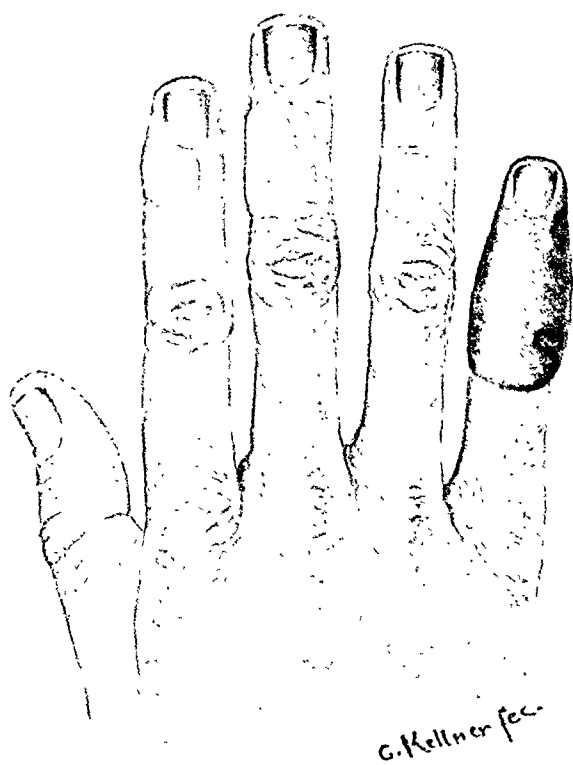
⁴⁴ Boston Med. and Surg. Jour., 1907, clvii, 247.

estimate nearly 500,000 people are attacked annually. It is more prevalent in country districts than in cities, and, as Fulton has shown, the propagation is largely from the country to the town."

The last census bulletin covers the year 1910, and it shows considerable improvement, the death-rate being 23.5 per 100,000. It is only in half a dozen eastern cities that our typhoid rates approach the low rates of the leading cities of western Europe, so that we have still much to do before the typhoid situation is at all satisfactory. Each year shows some improvement, as one community after another wakes up to the fact that investments in sanitation pay better interest than gold mines; nevertheless, improvements come at a snail's pace, and many generations must elapse before this country can equal England and north Germany in its freedom from typhoid. It is admitted that sanitary administration in this country has no organization; there is no national authority with power to compel obedience; even the States show no uniformity in their powers or standards. In this matter of sanitary administration we see the doctrine of home rule carried to the limit of absurdity. What can be done to protect against typhoid until such time as the Nation, the State, and our own communities shall give proper attention to sanitary problems, and guarantee to all that inalienable right the pursuit of health and happiness, free from the dangers of preventable disease. To illustrate our present dangers, one example will serve as well as another. Lumsden⁴⁵ has reported an outbreak of gastro-enteritis and typhoid among the passengers of a Mississippi river steamer. On July 29, 1912, about 1500 persons went on a Sunday school excursion. The day was warm, the steamer's water tanks small, and, to supply the demand, must often have been refilled from the river. Within a short time no less than 600 became ill of gastro-enteritis, and 13 cases of typhoid, with 3 deaths, were traced by Lumsden. As the disease was not reportable in either Iowa or Illinois, where this occurred, he felt certain that all had not been recorded.

This may serve to remind us that, at the present time, sanitation alone is not ample protection, and that some measure of personal prophylaxis is absolutely essential the moment we leave home. We are then reduced to measures of personal hygiene and individual prophylaxis, and the best method at the present time is vaccination. Only by it can we protect ourselves against infection with as great certainty as against smallpox; in this day and generation it is, in fact, the one promising method of protection from the sporadic and residual typhoid which has so far resisted the efforts of sanitarians. There is no occasion for conflict between the advocates of general and individual prophylaxis; one is as necessary as the

⁴⁵ Public Health Reports, Washington, 1912, xxvii, 1960.



Cutaneous Lesions on the Right Hand in a Fatal Case
of Streptococcus Septicemia.

other, and no one interested in the suppression of this disease can afford to ignore either.

All sound thinking people look forward to the time when National, State, and local health authorities will unite in a concerted movement for better sanitary conditions; unite in the fight against infectious diseases; when they will advance together along broad lines in the suppression of this scourge of civilization. In this campaign, antityphoid vaccination, as well as sanitation can, the writer feels sure, be counted upon to play a leading role.

CUTANEOUS MANIFESTATIONS OF SEPTICEMIA

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DESPITE the completeness of our knowledge of infection, there are a number of facts about the invasion of the body with microorganisms which defy explanation. Especially is this true of the selection of certain organs by one infective agent and their immunity from another. The susceptibility of the urethral mucosa to the gonococcus and the almost complete immunity of the vesical mucosa are well-known examples of this selective action. A similarly familiar instance is furnished by tuberculosis and syphilis of the genitalia, the affinity of the former for the epididymis, and the latter for the testicle being quite unexplained. A more striking instance still is the apparently absolute immunity of the prostate to syphilis; for though this disease may attack most of the tissues and organs in the body, no authentic instance of syphilitic prostatitis is on record, and the few reported cases in the literature will not bear scrutiny. A similar selective affinity is also exhibited by neoplasms. The female breast, so often the site of newgrowths, is almost immune to one of the commonest forms of neoplasm, the lipoma. In the rectum and pelvic colon, carcinoma is a frequent disease; yet in the adjacent hepatic flexure it is relatively rare. Whatever the explanation of these facts and others like them may be, it is certain that we must seek further than an irrelevant anatomical fact, like "a richer blood supply" or a "poorer blood supply," to account for them. Recent observations with the aniline dyes have shown how extraordinarily sensitive selective actions may be, and have suggested that chemotropism may play a part in the apparent vagaries of infection.

The pyogenic organisms, though fairly impartial in their ravages,

may in an individual case exhibit a choice of lodgment and symptoms out of the ordinary. These unusual symptoms are sometimes to be ascribed to known peculiarities of the invading organisms themselves. The phenomena, for instance, of streptococcic septicemia are not in general identical with those of staphylococcic septicemia; and an organism like *Bacillus aërogenes capsulatus* produces a septicemia which has features peculiar to itself. It seems not unlikely that *Bacillus mucosus capsulatus* tends to produce a septicemia of the hemorrhagic type; at least a number of observations of this kind are on record.

One of the unusual lesions of pyogenic septicemia, odd both in character and in site, was illustrated by a case of streptococcic septicemia which I saw a year ago in the New Haven Hospital. In this instance the lesions were unique in my experience. The patient, a Pole, aged fifty-nine years, had been struck on the head with a brick one week before admission, receiving a ragged laceration on the scalp in the right frontal region, near the hair line. The wound had been sutured by a physician. The patient had then gone on a week's drunk, and when next seen by his physician was found to be running a temperature of 102.5, and was sent to the hospital. On admission the edges of the scalp wound were found to be separated by necrotic tissue and the skull could be easily explored with the finger. No fracture was present. There was impaired resonance throughout the right back of the chest and the axilla, and coarse musical rales were heard throughout the right side. The temperature ranged around 102; muttering delirium soon developed, and a consolidation of the whole right lung was evident on the day following admission. The most striking feature, however, was the rapid development of the cutaneous lesions described below. *Streptococcus pyogenes* was isolated in pure culture from the blood and also from the fluid aspirated from the vesicle on the right little finger. The patient died from a streptococcic septicemia and double pneumonia seventy-two hours after admission.

The cutaneous lesions in this case are well represented in the accompanying illustration. For economy of space all the lesions are drawn on the same hand, though one was situated on the left hand. Scattered vesicles similar but less striking were also present on the feet. The rapidity of development of these lesions was a striking feature. The lesion on the little finger was found at rounds in the morning, though there had been no signs of it the night before. It seems probable that the lesions illustrated represent the evolution of the condition, and that it began as a bleb with a hyperemic base, containing clear fluid. The contents soon became blood-tinged, and finally (the whole process occupying but a few hours) a bulla filled with deep blue fluid resulted, as shown on the little finger in the drawing. This fluid lay between epidermis and dermis. The appearance was that of a thin finger-cot stretched

over the finger and distended with a blue fluid which could be seen shimmering through. The sharp edge of the lesion, with perfectly normal skin beyond, is shown in the illustration, and this feature has not been exaggerated by the artist. The lesion was an entirely intracutaneous one; there was no gangrene of the soft parts of the finger. Pure culture of *Streptococcus pyogenes* was obtained from fluid aspirated from the lesion.

The most familiar cutaneous manifestations of invasion of the body by microorganisms are the syphilides and (if a microorganism be conceded in this case) the exanthemas. In the class of diseases more strictly known as septicemia the following groups of cutaneous phenomena are to be distinguished:

1. *The Erythema Group.* Here are included the erythematous patches sometimes seen in the neighborhood of an infected joint or over an infected muscle. More striking is the "surgical scarlet fever" of Paget, Dieulafoy, Billroth, and others. In this condition a scarlet erythema, often fleeting but sometimes persistent, appears on the body following an operation, in an unclean area, often the mouth. The eruption may become papular, but angina is usually absent.

2. *Papular Rashes.* The rash may be originally papular or may become so after an initial erythematous stage.

3. *Urticarial Rashes.* The association of urticaria with toxic conditions is of course well known; there is evidence that toxins which are bacterial in origin may cause a rash of this kind.

4. *The Hemorrhagic Group.* The lesions vary from minute petechiæ to extensive purpuric stains. They may be confined to the skin or associated with hemorrhages in the retina and elsewhere. In some of the cases the involvement has been symmetrical (both arms and both legs); in others the whole body has been covered and the picture that of hemorrhagic variola. In a case reported by Litten, attention was called to the rapid evolution of the lesions, increase in size, and coalescence occurring under the artist's eyes with such rapidity that it was difficult for him to get a good picture. I have already mentioned that rapid evolution was a feature of my case. In some cases a pustule has formed at the centre of the purpuric spot.

Spotted hemorrhages in septicemia are of serious prognostic significance; they are more frequent in the bad cases, and according to Lenhartz have been present in about 50 per cent. of the fatal ones. Attention has already been called to the fact that *Bacillus mucosus capsulatus* seems to be rather prone to produce a septicemia of the hemorrhagic type.

5. *Vesicles, Pustules, and Pemphigoid Eruptions.* These are not frequent, though one may see them in association with the commoner rashes (erythema, roseola, urticaria, etc.), or one may see an evolution from one of the simpler exanthems, through a vesicular

stage to a pustular or pemphigoid eruption. Gussenbauer reported an urticaria following a septic gangrene of the lower leg, in which many of the lesions were transformed into vesicles containing bloody fluid. Bamberger was one of the first to report a case of pyemic pemphigus; since his publication the condition has been rarely seen, and only in cases of severe septicemia. When the eruption is vesicular the vesicles may arise from urticarial or ecchymotic spots, and may develop into pustules followed by ulceration. In a remarkable case reported by Unna the eruption was pock-like.

6. *Herpes*. Herpes labialis does not appear to have been a particularly frequent feature of pyogenic septicemia, to judge from the reported cases. This is rather surprising when one considers its frequency in diseases like typhoid fever, the exclusion of which from septicemia is purely a matter of nomenclature. Herpes labialis does, of course, occur in pyogenic septicemia; the statement that it is more common in toxic than septic conditions is probably in part due to the fact that when this has been the only cutaneous lesion present the case has not been considered interesting enough to report, and therefore has not gotten into the literature.

CONCLUSIONS DERIVED FROM FURTHER EXPERIENCE IN THE SURGICAL TREATMENT OF BRACHIAL BIRTH PALSY (ERB'S TYPE).

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IN 1905 Clark, Taylor, and Prout published¹ "A Study on Brachial Birth Palsy." The clinical portion of the study was based upon 7 operative cases. Since that time 36 additional cases have been operated upon, making 43 altogether. These have varied in age from four weeks to nineteen years.

Owing to the long lapse of time between the operation and the appearance of the end results in these as in many other cases of nerve suture (often two to three years) it has not been possible to follow many of the series as systematically and persistently as would be desirable for satisfactory case reports. Nevertheless the frequent operative contact with these lesions, the prolonged struggle involved in the after-treatment, and the constant con-

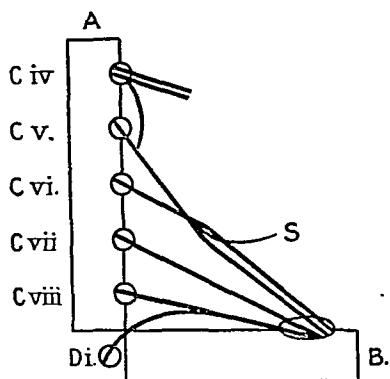
¹ AMER. JOUR. MED. SCI., October, 1905.

sideration of the problems involved have led to certain convictions which are worth presenting for discussion to those interested in this subject.

As to etiology there is no question that the chief factor lies in the forcible separation of the head and neck from the corresponding shoulder, whether it occurs through too forcible instrumental traction when the shoulders are impeded, or whether the head and neck are used to pry out the shoulder from under the pubis, or whether, in a breech, too great traction is put upon the shoulders for the delivery of the after-coming head.

A few mild cases of the palsy have occurred where spontaneous delivery has relieved both instruments and accoucheur of any participation as active etiologic factors. Such cases should render us loath to put the responsibility in any given instance upon the accoucheur, yet nevertheless he, by a proper grasp of the mechanics of the thing, can nearly always avoid doing, and can often prevent Nature from doing, what would tend to cause this very serious lesion. If any obstetrician will make a simple apparatus like Fig. 1 he can readily work out the essence of the etiology.

Fig. 1.—Schematic representation of brachial plexus. A, spinal column; B, shoulder; S, suprascapular nerve; C_{iv} to D_i, roots of plexus. If A and B are pulled away from each other C_v and C_{vi} would first be put on the stretch. After they had yielded C_{vii} would be involved, and so on down the line. S, the suprascapular nerve, would always be damaged first and most. If A and B are approximated the roots are relaxed, or if they have been torn the ends would be approximated. This should be the aim of treatment in all fresh cases.



In the original study only extraspinal lesions were considered. These, in brief, consist of rupture of the deep cervical fascia lying in front of the roots of the plexus, of rupture of the perineural sheaths, and finally of the nerves themselves, together with the vessels of all three structures. The resulting mass of torn fibrous tissue, nerves, vessels, and blood-clot organizes into a firm cicatrix which does not permit the passage of nerve impulses. The roots usually rupture in order from above downward, and the lesion involves one or more or all of them according to the degree of force used in causing the injury.

In addition to these extraspinal injuries there have undoubtedly been intraspinal lesions much more frequently than had been supposed. Where the roots are torn from the cord, hemorrhage occurs and the organization of the clot later causes cicatricial

deformity of the corresponding portion of the cord. This type of injury has been demonstrated by Dr. George Boyer, of Toronto,² in the case of a woman, aged forty years, who had borne such an injury through life.

It is not possible to state, with proof, that both extraspinal and intraspinal lesions occur in different roots of the same plexus, but the findings in certain of the cases operated upon most strongly indicate that such is the fact. For instance, in one of the late cases of the series there was a typical palsy of the upper arm type, fairly good motion about the elbow-joint, and complete flaccid paralysis of the hand, with marked atrophy of its intrinsic muscles. On dissection there was the usual cicatrix in the fifth and sixth roots extraspinally. The condition of the hand meant a serious lesion of the eighth cervical and first dorsal roots, but these, extraspinally, appeared undamaged, and on splitting their sheaths showed normal appearing fasciculi. There must therefore have been intraspinal damage to the two lowest roots of this plexus.

As previously stated the damage nearly always extends from above downward in the order of the roots, and involves from one to all the roots according to the degree of force used in causing the injury.

The damaged area in any given root may lie at any point between the spinal cord and the place where the final nerve trunks are given off from cords of the plexus. The lesion may consist of a circumscribed cicatrix involving a part or the whole of the root at any part of its course, or of several cicatrices scattered along its course, or of one large cicatrix involving practically the whole root. One cicatrix may involve two neighboring roots, this being commonly the case with the fifth and sixth roots, or may involve all the roots of the plexus when it has suffered complete rupture.

One or more of the roots may be completely torn across, the ends widely separated and grown fast to neighboring structures by scar tissue.

In all these cases the layer of deep cervical fascia lying just in front of the nerve roots is torn and always becomes adherent to the underlying nerves in the healing process. In certain rare cases the deep fascia alone is injured, adheres to the underlying nerves, and by cicatricial compression interferes with their functional activity.

With the exception of the intraspinal lesions, which could not be demonstrated anatomically, my series of 43 operative cases has illustrated each of the types above mentioned, and if one's operative experience were sufficiently extensive, he might expect to see an example of every type mathematically possible.

When the lesion is intraspinal, or when the cicatrix involves the

² *Pro. Royal Soc. Med.*, 1911 (Neurological Section), v, 31 to 56.

root well into the intervertebral canal, operation as at present performed offers little prospect of improvement. Whether some modification of procedure will benefit these cases remains to be seen. Implantation into a neighboring root has been tried in a recent case, but there has not been sufficient time for results to appear.

Following permanent interference with nerve function, certain secondary pathologic changes develop, the importance of which was not appreciated fully until after a considerable experience with the postoperative treatment of these cases, and which have a most decided bearing upon determining at what age surgical interference should be insisted upon. The bones of the extremity do not develop normally. The clavicle is small, the scapula is small, the coracoid process is often drawn downward and forward, forming a beak which interferes with free mobility of the joint, and the glenoid process maintains its infantile form. The upper end of the humerus remains infantile, and this, together with a similar condition in the glenoid process, renders easy the posterior dislocation seen in a certain proportion of these cases, which will be referred to later in dealing with symptomatology.

Constant maintenance of the elbow- and wrist-joints in the faulty positions characteristic of these cases causes the plastic bones of infancy to develop in somewhat abnormal shapes in their joint ends. Moreover, contractures in the paralyzed muscles and in the ligaments about the joints serve still further to fix and accentuate the deformities of the extremity as time goes on.

Thus the characteristic deformity seen just after birth is a purely functional one, and is due to the muscular imbalance resulting from the paralysis of certain groups of muscles. When, however, the paralysis persists through the early months or years of rapid growth the deformity, at first functional, becomes fixed mechanically by the organic secondary pathologic changes above enumerated. If late surgical intervention succeeds in obtaining good nerve regeneration, and this is usually the case, there still remain as serious obstacles to free motion these organic structural changes which enormously increase the period of postoperative treatment and prevent the attainment of a completely satisfactory ultimate result.

From this description of the incidence and sequence of pathologic events in these cases it is self-evident that in the great majority of instances there will be permanent interference with the transmission of nerve impulses in greater or less degree, and this degree will depend upon the number of roots torn and upon the distribution and extent of the resulting cicatrices. Inasmuch as the roots are almost always injured one after the other in order from above downward the muscles paralyzed naturally fall into the groups related to the primary roots of the plexus for innervation.

The great majority of the cases are of the "upper arm type," in which the injury involves the fifth and sixth roots. These two roots join soon after their exit from the intervertebral foramina, and this junction, which is often 1 cm. or more long, again divides to form trunks which enter into the plexus. From the outer edge of this junction is given off the suprascapular nerve. Injury to these roots is usually at their junction, or just above it, or at and just below it. In a smaller proportion of cases they are damaged at or within the intervertebral foramina, and rarely torn from the cord itself.

A study of the schematic plexus, Fig. 2 (Kocher), will indicate better than much description the muscle groups related to the different nerve roots and what must be the result of different root injuries.

While the schematic plexus is not accurately drawn a study of it will show how one may get some approximate idea of the situation of the lesion from the grouping of the symptoms. The branches to the deep muscles of the neck as well as those forming the posterior thoracic nerve come from the roots soon after their exit from the intervertebral foramina, so that if the rhomboids, the scaleni, and especially the serratus magnus are paralyzed one may deduce that the lesion extends up to if not into those foramina.

The more common lesion occurs distal to the origin of these branches, so that the winged scapula significant of serratus paralysis is not so frequently seen.

The usual picture in the newborn child is that of a complete flaccid paralysis of the extremity which lies close along the side with the elbow and wrist straight and the fingers somewhat flexed. There is marked inward rotation of the entire extremity, with pronation of the hand. This total paralysis results from the fact that those nerves which have not been torn and permanently injured have been overstretched and temporarily paralyzed.

In the not rare cases where the entire plexus is ruptured this clinical picture is permanent. In the less severe cases the lower roots begin to functionate, so that after days or weeks, as the case may be, motion begins to appear first in the fingers, then in the hand, wrist, forearm, etc., up to the level of the permanent lesion. In still slighter cases these motions in the distal portions of the extremity may be present from the start.

As time goes on the permanently paralyzed muscles undergo contracture and cause the typical deformity seen in Fig. 3; they also atrophy. This atrophy is not so easily made out in the young infant because of the thick layer of subcutaneous fat which keeps the form of the extremity filled out.

In certain of these cases there develops after a time a posterior luxation or subluxation of the shoulder-joint. This results from a combination of factors. The complete paralysis of the spinati

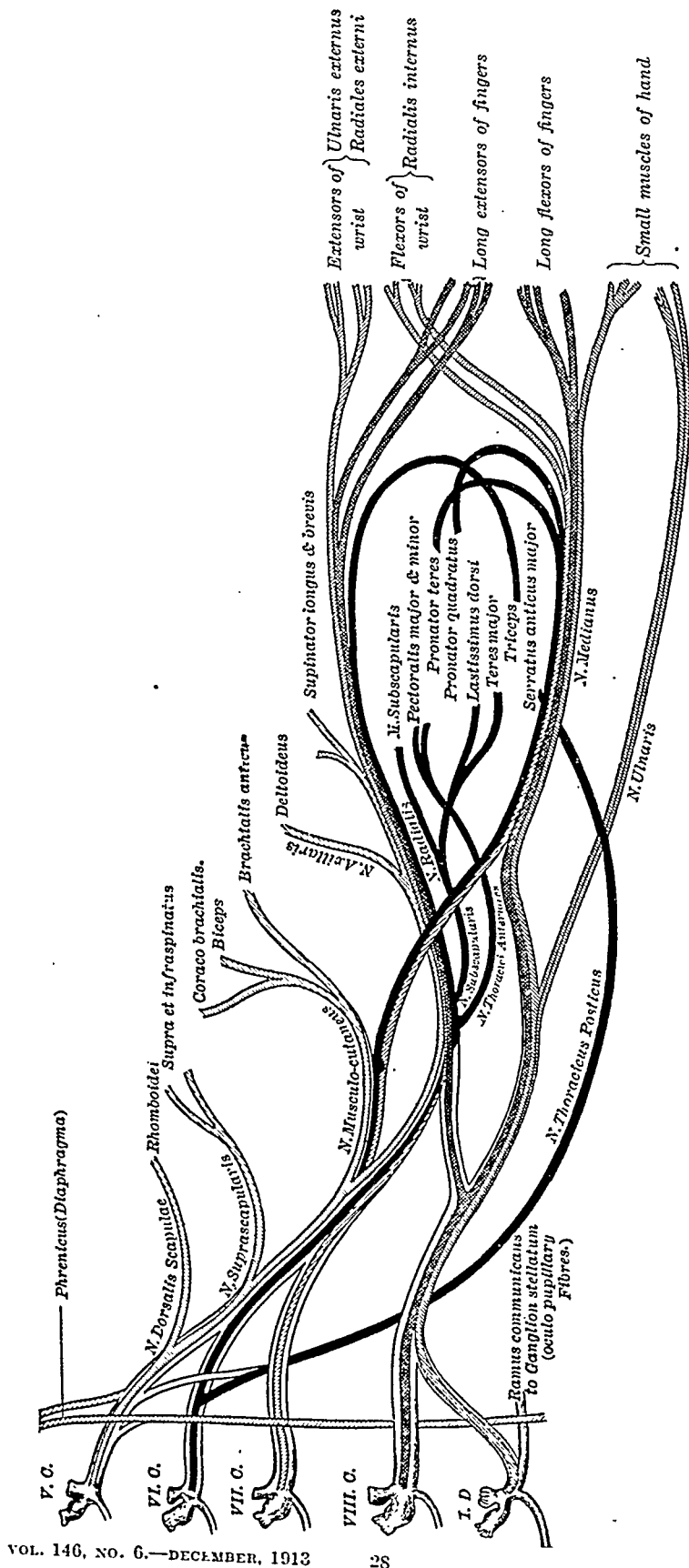


FIG. 2.—Schematic diagram (Kocher) to show the formation of the brachial plexus and the nerve supply to the muscles of the upper extremity.

and deltoid leaves the posterior and external aspects of the joint without the usual muscular support. The persistent infantile shape of the glenoid fossa and the end of the humerus favor easy dislocation. The pectoralis major, being usually only partially paralyzed, strongly rotates the humerus inward and exerts some pressure backward upon it. When the subscapularis, teres major, and latissimus dorsi escape partially or wholly from the paralysis they add much to the inward rotation and posterior displacement of the upper end of the humerus.



FIG. 3.—Typical deformity in a late case. Note the small size of the entire extremity, the marked inward rotation and pronation, the flexion at the elbow, the marked flexion, and ulnar adduction at the wrist.

This posterior displacement occurs in greater or less degree in every case, and can be made out readily by careful comparison with the opposite normal shoulder. The extreme degree of this displacement results in complete posterior luxation. When the biceps and coracobrachialis suffer from contracture there is an added upward thrust to the head of the humerus which brings it well up under the acromion process.

In the literature these complete posterior dislocations not infrequently appear under the title of "Congenital Posterior Dislocation of the Shoulder." One Boston, one Philadelphia, and one

New York case are on record in which operative procedures upon the shoulder-joint itself were done, with the idea of reducing the dislocation. In one of the three where reduction was impossible the head of the humerus was resected.

The histories, the pictures of the characteristic attitudes of the extremities, and the results in these cases leave practically no doubt that they were really examples of brachial plexus injury at the time of birth. These cases accent the necessity of the surgeon's associating a neurologist with himself in the care of these obscure congenital deformities about the shoulder-joint.

From infants it is practically impossible to derive any satisfactory information as to sensory disturbances in these arms, and by the time they are old enough to examine satisfactorily, sensory disturbances have disappeared except possibly in the cases of severe injury where some hypesthesia or anesthesia may persist.

There is regularly interference with the growth of the extremity.

One symptom which was worked out by Clark and presented in the original study is not sufficiently comprehended and appreciated. Careful palpation of the region of the fifth, sixth, and seventh transverse processes invariably makes out a characteristic induration which varies with the severity of the lesion, and which is always sensitive to pressure. The examiner should approach the sitting child from the rear and palpate both sides of the neck at the same time to compare the normal with the damaged side.

This induration seems to be less marked in those cases where the roots have apparently been pulled from the cord.

The meat of this problem lies in the question of prognosis in these cases when they are not treated surgically. Upon a proper conception of the prognosis must depend the system of treatment which will lead to the best ultimate results.

Most text-books give an optimistic prognosis. For instance a well-known pediatric text-book says: "The great majority of cases recover spontaneously in two or three months, improvement being observed within a few weeks. Spontaneous recovery is not to be looked for unless it occurs within the first three months. Not infrequently some degree of paralysis persists until the third or fourth year, and in some of the muscles, especially the deltoid, it may even be permanent."

A well-known text-book on neurology says: "Many of these cases go on to spontaneous recovery within six months after birth. Others remain longer and do not recover within the first year. The condition may remain for three or four years and pass away only when the child is old enough to be taught systematic gymnastic exercises."

These quotations are evidently optimistic. As a matter of fact in all these unfortunates (except where the entire plexus has been

ruptured) spontaneous improvement appears after an interval of three to twelve weeks after birth and continues slowly until the child is about two years old. After this time improvement ceases and the pathologic sequels previously mentioned cause increasing deformity and interference with function.

This long period of time over which spontaneous improvement occurs is to my mind the chief cause of the firmly fixed but entirely erroneous belief with regard to the prognosis in these cases. The mothers take their infants to the clinics, are told that the outlook in most instances is good, and are invited to come regularly for manipulation and electricity. After a time improvement sets in and progresses steadily. After a further interval, pressed by other demands upon her time and relieved of her mental anxiety by the prognosis of ultimate spontaneous recovery, the mother ceases to attend the clinic. The physician, looking over his records, and remembering the continuous improvement over a period of time, attributes the further non-attendance to spontaneous recovery. If, however, he would visit any of the orthopedic dispensaries he would find many of these children applying for treatment at a time when the mothers had given up hope of the recovery which had been held out to them in the infancy of the victims.

Recently a child, one year old, was brought in by its mother. It had a marked paralysis still persisting with absolute flaccid paralysis of the wrist and hand. Yet when this child was only three months old he was taken to one of our well-known neurologists, who examined him and then told the mother to rub the arm, put it through passive motions for the joints, and it would come around all right. The hopelessly crippled extremity at the end of a year led the mother to consult an orthopedic surgeon, who referred him for immediate operation. At operation C VI, VII, VIII, and D I were completely torn across and regeneration could never have occurred.

This kind of history is repeated again and again in our operative cases, and this attitude on the part of the profession at large does more than anything else to prevent these unfortunate cripples from obtaining the best treatment at the best time.

Let me say, with as much emphasis as possible, that my personal experience convinces me that the prognosis in these brachial injuries is exceedingly bad; that complete spontaneous recovery is rare, occurs only in mild cases, is complete usually by the end of three months, and almost never later than six months. In the vast majority of cases there will be a permanent defect.

Until the true prognosis permeates the general profession the surgical repair of these lesions will never have its best opportunity, and anyone who follows these cases for a sufficient length of time will become convinced that surgery alone holds out the best hope to the great majority of them.

Having arrived thus far the one great thing is to choose the best time for operative interference.

It is generally admitted that nerve generation and regeneration are most active in young infants.

Here as elsewhere in the peripheral nervous system the sooner a divided nerve is sutured end to end the better is the prospect of a satisfactory result.

Within a few weeks or months of birth the secondary pathologic changes previously enumerated begin to develop, causing a mechanical fixation of the extremity in its deformed attitude. The longer this fixation has persisted the more tedious will be the after-treatment.

From the above premises the only logical deduction would be immediate operation. However there are some reasons for temporary delay. It is unwise to subject a newborn babe to anesthesia until it has had a short time to adjust itself to its new surroundings and to show how competent its digestive apparatus is to be.

The damaged tissues should have time to regain their normal resistance to infection. Instead therefore of demanding immediate operation, which would be best from the standpoint of nerve repair, we must demand operation at the earliest feasible moment considering the general condition and the local resistance of the individual child. Under these circumstances the choice of time for operative interference may vary from two weeks to three months. Seldom will it need to be postponed beyond three months.

It will be noted that in laying down the indications for operation nothing has been said with reference to spontaneous regeneration and recovery. The plan of waiting until spontaneous improvement has ceased is the greatest imaginable stumbling block in the way of obtaining the best results in this whole class of patients, for the reasons mentioned under "secondary pathologic changes." In all cases where a really complete spontaneous recovery will occur the primary paralysis will be of only moderate degree and obvious improvement will begin within the first couple of weeks. In every case where there is considerable paralysis and where no improvement begins within the first few weeks there is certain to be some degree of permanent injury to the roots.

In every case where this permanent injury is indicated, and in every case where it is even debatable whether permanent injury has occurred, operation at the earliest feasible moment, as above indicated, should be performed.

In these operations the chief risk lies in the anesthetic, because the wound goes only through skin and fatty tissues; with experience the loss of blood may be limited to one or two teaspoonfuls; the shock is negligible, and the time consumed varies with the complexity of the lesion found.

In the debatable cases the procedure might better be called an

exploration rather than an operation. If no lesion demanding nerve resection and suture be found the wound is promptly closed and the whole thing is over in fifteen minutes, with no chance of harm to the child. It amounts to nothing more than the making and closing a skin incision, which permits inspection and palpation of the roots, with precise knowledge upon which to found the after-treatment for the individual case.

If on the other hand a definite lesion is found it is resected and followed by end-to-end suture, and this is done at the time which is obviously the best for the child's future.

The newborn victim of this injury is caused to suffer much pain and detriment because of the advice commonly given to the parents—namely, "to start at once with massage, passive motion, and (possibly) electricity."

One should remember that the original injury starts a traumatic neuritis, which is aggravated by massage and passive motion, especially about the shoulder region. This added irritation causes more scar tissue to interfere with nerve regeneration. Moreover, the victim is caused an unnecessary amount of pain.

In all these cases the best primary treatment would be to keep the injured extremity at rest for at least two weeks. This might best be done with an ordinary triangular sling so arranged as to derive all its support from the sound shoulder and to cause marked elevation of the shoulder on the damaged side. This method obviously removes all strain from the plexus, and, in case any of the roots are torn, approximates the ends and gives the best opportunity for spontaneous repair.

At the end of two weeks the sling may be removed daily and gentle massage given, always with care not to pull the shoulder away from the head and neck, as this would again stretch the damaged nerves.

At the end of three weeks decision should be made for or against operative exploration, and, if operation is chosen, it should be done as soon as the particular child can stand it.

Some variations from the operative technique published in the original study may be worth mentioning.

In extensive lesions the incision there described, running from the lower third of the sternomastoid to the outer third of the clavicle, gives the best working exposure. For less extensive cases, and in young children where the tissues are elastic, an incision from the insertion of the sternomastoid running outward and slightly upward, following the natural wrinkles in the skin at the base of the neck, will give a satisfactory exposure, and heals with a scar that will never spread. The first incision heals by primary union satisfactorily, but later always spreads into a broad, flat, white scar, which is objectionable in females.

Where there will be tension on the nerve suture, silk is the preferred material. In young infants in whom the working space and the nerves are small, and where there is less likelihood of much tension on the sutures, a purse-string suture of fine chromic catgut answers.

In infants a few weeks old the dissection is comparatively easy because the scar tissues have not become firm and the nerves are readily identified. Apposition is also easier.

The older the child the firmer the scar tissues become, and the more difficult is the dissection. In some of the older cases, where some of the roots have been torn completely across, the ends displaced and later bound by firm adhesions to neighboring structures, a field for dissection is provided in which the greatest patience, endurance, and skill in anatomical orientation is requisite to ravel out the mysteries contained in the blanket of scar tissue.

In those cases where a root or roots have been torn from the cord they must be anastomosed into a neighboring root, with the hope of getting a distribution of power. This procedure has been done within the last few weeks in a child and in an adult after an avulsion of the C VIII and D I from the cord.

When the nerve sutures are placed, and if there is more than one they must all be placed before any of them are tied, the head, neck, and shoulder are approximated. This position must be maintained without a moment's relaxation. The sutures are tied from below upward, the skin wound is closed with silk, a sterile dressing applied, and appropriate fixation accomplished. This fixation apparatus must hold the head and shoulder in close approximation without a moment's cessation for from three to twelve weeks from the time of operation, according to the individual case.

In the early cases a plaster splint, fashioned before operation, was used, but it proved not only to be heavy, clumsy, and uncomfortable, but, worst of all, after ten days became so limp as no longer to maintain the necessary position.

A steel brace was then devised (Fig. 4), and this has served its purpose without undue discomfort to the patient. In the case of young children, when it is properly applied, it permits free handling for bathing and dressing, and is not much in the way of the clothing.

The brace is made of flat steel rod appropriately bent and supplied with supports for the forearm and shoulder. A muslin cap is fitted to the child's head, the edges of which are turned up over the head part of the brace (Fig. 5). This prevents the head from protruding too far through the brace. An adhesive plaster strap is started from the top of this cap, passes down the cheek of the well side, and across under the chin to the shoulder pad of the brace. The shoulder pad, which overlies the scapula of the damaged extremity, is fastened by a broad adhesive strap which passes from

the pad obliquely downward over the child's back (Fig. 6). The forearm and arm are bandaged to the brace.

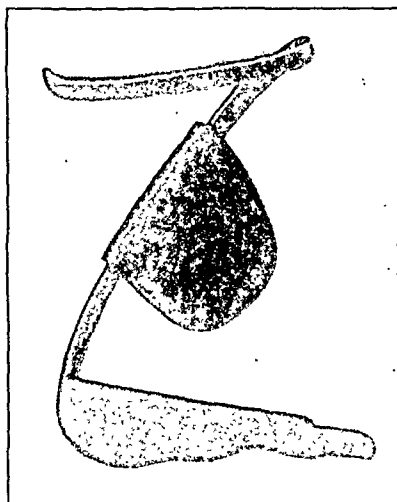


FIG. 4.—Steel brace, showing grooved channel for the forearm and hand, a large pad to hold the shoulder forward, and the upper curved band to encircle three-quarters of the head. The whole thing is padded and covered with leather.



FIG. 5.—The brace applied, elevates the whole extremity so as to approximate the shoulder to the neck. The upper part, with a muslin cap stitched to it, holds the head down and to the damaged side. The chin strap prevents the child from getting its head out from under the brace. The shoulder pad, fitting over the scapula, holds the shoulder from being displaced backward. The net result is to hold the child fast with the head and neck and shoulder closely approximated so as to relieve the strain on the nerve sutures. This position is the one that should be adopted in every fresh case so as to approximate the damaged nerve ends and give the best chance for spontaneous healing.

This brace must be carefully fitted and adjusted before operation, or pressure sores are apt to develop and complicate the postoperative treatment.

Many parents and even practitioners express the fear that wry-neck will follow the prolonged fixation of the neck. In my whole series of cases that complication has not appeared a single time.

The after-treatment is an exceedingly important part of the care of these children. It starts with the removal of the brace, and at first should consist of massage and passive motion applied to the fingers, hand, wrist, forearm, elbow, and muscles of the arm. For an interval of four to six months after the operation, manipulation about the base of the neck and shoulder should be used with great care to avoid putting strain upon the sutured nerve roots. For the same reason such manipulation as is given to the remainder of the extremity should always be conducted in a way not to pull the shoulder away from the neck or downward.



FIG. 6.—Showing the posterior view of the brace, with a broad band of adhesive plaster running from the shoulder pad obliquely down across the back. The cap, which was just pinned on for the picture, has become distorted in the child's wriggling.

Electricity, while not essential, is of some value, and often helps to keep the parents at systematic treatment.

After sufficient time has elapsed for absolutely firm union to have occurred in the sutured roots, manipulations about the shoulder should be more vigorous. The greatest difficulty to overcome lies in the contracted pectoralis major and the shortened anterior capsule of the joint. It may be necessary to stretch them under an anesthetic or to lengthen the pectoralis tendon. These troubles ensue only in the cases which have been too long neglected before operation.

As the evidences of nerve regeneration appear the child must be educated to use the muscles, heretofore functionless, by means

of gymnastic exercises, games, workshop methods, etc. These methods must be followed systematically for several years to get the best results after operation.

The first question asked always is, What are your results?

To allay any suspicion of overenthusiasm or radicalism I may state frankly that I never have seen a perfect arm result from operation nor do I ever expect to. There is always failure to reach perfect function to a greater or less degree.

On the other hand in the great majority of cases there will result a degree of improvement which can be attained by no other method than the surgical repair of the damaged nerve roots. Several of the series operated upon had been given systematic physical therapeutics over a period of two years, with so little result that the parents turned to operation as a last resort. The results were a great improvement over anything obtained by the previous efforts.

If the operative technique and after-treatment are properly carried out the results will always be worth the trouble.

Instead of publishing a long list of case histories I shall illustrate the value of operation by detailing one case, with serial photographs, in which the entire result must be credited to the surgical interference because there had been complete rupture of the plexus, and there had been absolutely no spontaneous improvement during the year of life.

Ruth F. (Case 9 of my series), aged one year.

History. She was the second child of the family, was large, and was delivered with instruments after a difficult labor. Soon after birth it was noticed that the left upper extremity was lifeless. There has never been any improvement in it in spite of intermittent treatment received in various clinics. Except for the arm she has been perfectly well.

Examination. She is a large, well-nourished child, normal except for the left upper extremity, which hangs lifeless by her side (Fig. 7). There is some power in the serratus magnus, contraction of which, with some contortion of the trunk, throws the extremity slightly forward. The soft tissues are flabby and the extremity is cold. The muscles show reaction of degeneration. A large indurated mass can be felt on the left side of the neck at the site of the brachial plexus.

Operation. June 8, 1905. Ether anesthesia. The plexus was exposed by the usual dissection. The deep fascia was thick and adherent to the front of the whole plexus, which was itself one large mass of cicatricial tissue, with the nerve roots running into it above and the nerve trunks coming off from it beneath the clavicle. The roots were divided above the cicatricial mass nearly at the foramina. The plexus was removed *en masse* by dividing the nerve trunks as they emerged from its distal end beneath the

clavicle. In attempting end-to-end suture the nerve ends could be approximated to within only 2 cm. of each other, so loops of chromic gut (No. 1, 40 day) were passed through the roots and distal trunks and surrounded *en masse* with cargile membrane. The suprascapular nerve was carefully included in the suture. The wound was closed without drainage and the head and neck bound in close approximation. This fixation was maintained six weeks. (At the present time I should hold the position for at least twelve weeks, which I could easily do with the steel brace.) The reaction was good. Primary union resulted.



FIG. 7.—Rupture of the entire plexus on the left side. Note the completely paralyzed, flaccid hang of the left extremity while she is playing with something in the right hand.

Postoperative History. This child was brought for examination only at irregular and infrequent intervals. At the end of three months the muscles were more flabby than ever, the shoulder was a flail-joint, and there was no sign of returning power.

December 21, 1905, six months after operation, the mother first noticed that the terminal joints of the thumb and index, middle, and ring fingers were swollen, glossy, red, and ulcerated on the tips. They were not sensitive and were not infected. They remained in this condition for about six weeks, and then gradually the fingers improved, until, on May 21, 1906, they were almost normal again.

While this trophic disturbance was present in the digits, there

was, on December 21, 1905, distinct but slight activity in the pectoralis major, triceps, and serratus muscles.

May 21, 1906 (one year less eighteen days), the movement in the above muscles was stronger. There also appeared some power



FIG. 8.—Eleven and one-half months after operation.



FIG. 9.—Same as Fig. 8. Lying on her back she is able to raise the arm perpendicularly.

in the deltoid, both for anterior elevation of the arm and slightly for abduction (Fig. 8). There was also slight power of flexion at the wrist. When she was lying supine she could elevate the entire extremity to a perpendicular with the floor without much effort

(Fig. 9). At this time there was distinct contracture of the flexor muscles of the fingers. The mother had neglected the massage. The shoulder had lost its flail-like character and the muscles of the whole extremity were firmer.

October 27, 1907 (two years and four months). The flexion contracture of the fingers had entirely disappeared. She had been using the extremity freely for the preceding six months,



FIG. 10.—Sixteen and a half months after operation. Note the improved size and position of the hand and arm.



FIG. 11.—Same as Fig. 10. Voluntary flexion at the elbow with some supination of the forearm.

handling playthings, feeding herself with it, etc. All of the muscles showed some return of voluntary power, although the flexors of the fingers and extensors of the radial carpus were quite feeble. The extremity had grown very well.

February 4, 1908 (two years and eight months). Marked improvement in all the movements of the extremity. She can put the hand to the mouth easily. There is fairly strong flexion and extension of all the digits.

February 1, 1910 (four years eight months). Marked increase in power of muscles. Can do things with the separate fingers.

February 7, 1911 (five years eight months). Marked increase in power and definite control of the muscles. The whole extremity is smaller than the right one.

SUMMARY. The essential etiologic factor consists in the forcible separation of the head and neck from the shoulder on the side of the lesion.



FIG. 12.—Same as Fig. 10. Anterior elevation of the extremity so that wrist is at the level of the hair line. The hand is still useless.



FIG. 13.—Same as Fig. 10. Abduction at the shoulder showing activity of the deltoid.

Pathology. The deep cervical fascia, the nerve sheaths, the nerves, and small accompanying vessels are torn. After a time the resulting blood-clot and torn structures form a dense cicatrix which prevents nerve regeneration. As a rule the injury involves the roots in order from above downward, and may vary in extent from a slight injury of the upper root to a complete rupture of the entire plexus. In some cases roots are torn from the cord itself. Secondary pathologic changes occur in the muscles, ligaments, and joint-ends of the bones.

Symptoms. The paralyzed muscles fall into groups according to the roots injured. The characteristic attitude is one of marked inward rotation of the whole extremity, which is accentuated by the pronation of the forearm and hand. There is always some posterior displacement of the upper end of the humerus as compared with the normal side, and in a small proportion of cases there is complete posterior dislocation of the shoulder. Sensory disturbances are slight and usually soon disappear. Interference with growth



FIG. 14.—Three years after operation. Showing growth of arm and hand.



FIG. 15.—Same as Fig. 14. Showing sufficient strength to support a large heavy doll upon the forearm and hand.

is always present and is most marked about the shoulder girdle. Deformity usually increases with age. A cicatrix can easily be felt in the region of the damaged nerves, and is usually tender even after years.

Prognosis. Prognosis is bad. There is nearly always some degree of deformity and paralysis which persists.

Operation. Operation gives the best prospect for a useful arm. The best time for operation is as early as the general condition of the individual patient will permit (three to twelve weeks). In

the few cases in which complete spontaneous recovery will occur the paralysis is usually not extensive, improvement starts early and continues rapidly, and operation is evidently contraindicated. In debatable cases operation really amounts to early exploration, with repair of such damage as may be found. There is exceedingly little danger to the operation, which amounts only to an incision through the skin and fat at the base of the neck.



FIG. 16.—Same as Fig. 14. A light rubber doll grasped in the hand (that is, lifted from a chair by the left hand) and held forward of the body with the elbow flexed. This child had a complete rupture of the plexus and complete flaccid paralysis of the whole extremity.

Up to the time of operation the extremity should be held up in a sling to take its weight off the damaged nerves and paralyzed muscles.

In the cases where roots have been torn from the cord they must be laterally implanted into the neighboring roots, or if the neighboring roots have been damaged enough to require resection all of the distal nerve trunks may be sutured in a bunch to the proximal roots still attached to the cord.

After operation the head and shoulder must be held in approximation for weeks by a steel brace fitted before operation.

After-treatment must be systematic and persistent.

Results will never be perfect, but operation will give improvement much greater than that obtainable by any other method.

FURTHER EXPERIENCES WITH STRETCHING OF THE PYLORUS.

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IN four¹ previous papers I have shown that the pylorus can be stretched by way of the mouth. I have described the necessary technique and reported a number of cases treated by this method.

In the present article I purpose reviewing briefly the old cases in whom the pylorus had been stretched, with regard to their results, and then to report my new experiences along this line. Altogether, there were 12 cases in grown people and 3 in infants, in whom the pylorus was widened. Of the infants, 2 were cured and remained well, 1 died about ten days afterward, that is, the stretching did not accomplish the desired benefit.

Of the 12 grown patients 9 remained well, 1 had a perforation of the diagnosed duodenal ulcer (Miss J. C. C.) two years after treatment and was operated successfully, 2 died: 1 about a year later from the results of a gastric hemorrhage (H. T.), the other (Dr. F. L. C.) from a return of the stricture of the pylorus. He was advised to be operated, but refused and succumbed some months later.

The new cases treated during 1912 and up to July, 1913, have been embodied in the subjoined table, and but three of them are here described.

By referring to the table, it will be found that the pylorus was stretched in 21 patients.² The number of stretchings amounted to 100. In 3 patients [E. C. A. (5), W. J. McC. (13), and Rev. M. J. D. (6)] the pylorus had to be stretched over the thread by means of the pyloric dilating catheter, for the pylorus was too narrow to admit the passage of the usual pyloric dilator. In patient Rev. M. J. D. the latter instrument could then be employed. In two patients (Rev. W. H. W. (2) and A. D. S. (7) the double balloon pyloric dilator was used off and on, in order to stretch the pylorus *in situ* for a somewhat longer time (one to two minutes). This mode of stretching is more effectual, but at the same time more difficult to accomplish. The patient is compelled to swallow a somewhat larger instrument and the physician has to know the exact amount of air which he may instill into the dilating balloon.

¹ Max Einhorn, Dilatation of the Stomach and Chronic Benign Ischochymia, Illinois, Med. Jour., June, 1910; On Pylorospasm, Med. Rec., January 21, 1911. Stretching of the Pylorus in Benign Stenosis, Med. Rec., June 10, 1911; Widening the Pylorus without Operation, New York Med. Jour., May 11, 1912.

² Nineteen entirely new, and three (Cases 1, 3, and 8) which had been described before, but in which the stretching of the pylorus was continued during 1912.

TABLE OF NEW CASES IN WHOM THE PYLORUS WAS STRETCHED.

No.	Name.	Diagnosis.	Gastric secretion.	Isochymia or hypersecretion.	Date of stretching and size of pylorus.	Result.	Remarks.
1	Dr. L. C.	Dilatation of stomach; benign stenosis of pylorus	HCl + Acid = 75	Slight isochymia and considerable hypersecretion present.	1911—Oct. 17, 21, 24, 31 (50 mm.); Nov. 13 (52 mm.), 24 (55); Dec. 22, 28, —Jan. 9 (60 mm.); Feb. 19; March 3, 24 not passable; April 1, 3, 16; May 7.	Good; stomach regained almost normal motility up to March; then relapse.	Patient had first gained twenty-three pounds, but later grew worse.
2	Rev. W. H. W.	Ulcer of the stomach; pylorospasm.	HCl + Acid = 90	Slight hypersecretion present.	1911—Nov. 16, Dec. 3, 1912—Jan. 2, 16 (46 mm.); Feb. 15, (50 mm.); Mar. 6, April 18, May 23.	Good; pains and hypersecretion ceased.	
3	Mrs. B.	Gastric ulcer. Dilatation of stomach, with benign stenosis of pylorus; movable kidney.	HCl + Acid = 48	Slight isochymia present.	1912—Jan. 5 (38 mm.), 10 (40 mm.), 18 (44 mm.); 30 (44 mm.); Feb. 21 (50 mm.).	Normal motility; gained fifteen pounds in 3 months.	
4	Miss F.	Gastric ulcer; dilatation of stomach; pylorospasm.	HCl + Acid = 75	Neither isochymia nor hypersecretion present.	1912—Jan. 11 (60 mm.).	Felt better; gained some.	
5	E. C. A.	Benign far-advanced stricture of pylorus; cirrhosis of liver.	HCl + Acid = 80	Pronounced isochymia present.	1912—Feb. 3, 17, 24; Mar. 2.	Good; good motility reestablished; gained twenty pounds.	The stretching was done over the thread with the dilating catheter.
6	Rev. M. J. D.	Ulcer of the stomach; benign stenosis of the pylorus.	HCl + Acid = 100	Continuous hypersecretion present.	1912—Feb. 6, 23 (52 mm.), 28 (50 mm.); Mar. 5 (54 mm.), 12 (50 mm.), 29 (52 mm.), April 16 (55 mm.); May 7 (55 mm.), 28 (52 mm.); Oct. 9, (56 mm.).	Good; no pain; stomach empty when fasting.	
7	A. D. S.	Ulcer and dilatation of the stomach, with pronounced pylorospasm.	HCl + Acid = 116	Continuous hypersecretion and slight isochymia present.	1912—Mar. 12, (50 mm.), 15 (56 mm.), 19 (66 mm.), 28 (56 mm.); April 7, 17 (65 mm.), May 12 (55 mm.), 19 (74 mm.), 26; June 3, 17 (60 mm.), 29 (69 mm.); Nov. 17 (56 mm.), 24 (60 mm.); Dec. 1 (70 mm.), 15 (70 mm.). 1913—Jan. 5, 12, 19, 26 (61 mm.); Feb. 15 (70 mm.).	Good; with regard to gastric motility.	Three months after the last stretching patient had a severe gastric hemorrhage. He was operated on three weeks later, beginning of July, and made a good recovery.
8	Mrs. H. H. W.	Anemia; gastric ulcer; beginning stenosis of pylorus.	HCl + Acid = 60	Neither isochymia nor hypersecretion present.	1912—Feb. 23 (40 mm.); Mar. 4 (52 mm.); Sept. 26 (42 mm.), 28, 29 (45 mm.).	Good, free from pain, regained ten pounds in weight.	

9	E. S. M.	Bradycardia, dilatation of stomach and pylorospasm.	HCl + Acid = 96	Continuous hypersecretion present.	1012—April 10 (51 mm.).	Good.	
10	Eugene F.	Ulcer of stomach and pylorospasm.	HCl + Acid = 80	Continuous hypersecretion present.	1912—April 30 (49 mm.); May 12 (70 mm.).	Improved; pains less severe, but still present. Good with regard to pylorus; no pain; gained in flesh.	About five months after the last stretching had a gastric hemorrhage; operated by Dr. Blake; recovery.
11	E. C. M.	Gastric ulcer and beginning benign stenosis of pylorus.	HCl + Acid = 96	Continuous hypersecretion present.	1912—May 24 (38 mm.), 27 (46 mm.); June 14 (50 mm.), 27 (51 mm.); Sept. 10 (48 mm.); Oct. 1 (52 mm.), 18 (51 mm.).		
12	H. P. R.	Ulcer of stomach; gastralgia tarda; pylorospasm.	HCl + Acid = 75	No.	1912—May 14 (50 mm.), 17 (51 mm.), 21 (46 mm.); Sept. 13 (52 mm.).	Good, free from distress, gain in weight.	
13	W. J. McK.	Dilatation of stomach; stenosis pylori benigna; peristaltic restlessness; cirrhosis of liver	HCl + Acid = 90	Pronounced isochymia present.	1912—May 28 (38 mm.).	Good temporarily in widening the pylorus and making duodenal feeding possible.	Patient was operated later by Dr. Willy Meyer; recovery.
14	Henry B.	Gastric ulcer; beginning stenosis of pylorus.	HCl + Acid = 70	No isochymia.	1912—Sept. 24 (41 mm.), 28 (50 mm.); Dec 15 (60 mm.), 19 (65 mm.); 1910—Oct. 20 (51 mm.).	Good, no pain, gain in flesh.	
15	Henry T.	Gastric ulcer near pylorus; pylorospasm.	HCl + Acid = 86	Continuous hypersecretion present at times.			
16	Marshall McK.	Dilatation of stomach and gastric ulcer.	HCl + Acid = 55	Continuous hypersecretion present at times.	1912—Nov. 26 (60 mm.), 29 (62 mm.).	Good.	
17	G. J. R.	Duodenal ulcer; gastralgia tarda.	HCl + Acid = 85	Continuous hypersecretion present at times.	1913—Jan. 30 (55 mm.); Feb. 4 (58 mm.).	Good.	
18	Harold Du C.	Gastralgia	HCl + Acid = 65	No.	1911—May 18 (52 mm.).	Good.	
19	Frank D.	Ulcer of stomach near pylorus; pylorospasm.	HCl = 55 T.a.c. = 68	Isochymia present in a small degree.	1913—May 6 (51 mm.), 13 (55 mm.).	Gastric motility good; gained in weight.	
20	Nicolas ² de C.	Enterit. chr. dilatation of stomach; pylorospasm.	HCl + Acid = 96	No.	1913—June 17 (60 mm.), 24 (65 mm.).	Good.	
21	Solomon M.	Dilatation of stomach and pylorospasm.	HCl + Acid = 100	Continuous hypersecretion present.	1913—April 1 (60 mm.), 8 (62 mm.); May 6 (60 mm.), 20 (62 mm.).	Good; no pains; gained in weight.	

Among the patients treated by stretching, 8 had a real stenosis of the pylorus while 13 suffered from pylorospasm of varying severity.

In all my experiences with stretching of the pylorus, I have thus far encountered no mishap whatever. Two or three times the dilating balloon was somewhat tinged with blood, due to an ulcer situated in the pyloric vicinity, but even then there were no ill results.

The results were, as a whole, very good. The pains subsided and the ischochymia or hypersecretion, if present, decreased or disappeared.

Two of the patients reported in the table [E. C. M. (11) and A. D. S. (7)] improved with regard to their pylorus, but had, several months after the stretching, due to the presence of their ulcers, a return of gastric hemorrhages. Operation was performed in both by prominent surgeons, in one by Dr. Kammerer and in the other by Dr. Blake, with complete recovery.

As examples, we single out two cases of real pyloric stenosis and one of pylorospasm which we shall briefly describe:

CASE I.—Cirrhosis of the liver and dilatation of the stomach and benign pyloric obstruction. W. J. McC. (13), aged about fifty-two years, began to be troubled with digestive symptoms about five years ago. Pains two to three hours after meals and occasionally vomiting were the chief complaints. After three years, which contained periods of suffering intermingled with intervals of euphoria, he went to Vichy and later to Nice, France, where he was treated by gastric lavage and a strict milk diet. He then lost considerably in weight, but, as a whole, felt better for a while. During the last six months, before consulting me, the patient was suffering all the time, frequently vomiting large quantities of gastric juice, with some food. He had meanwhile lost over sixty pounds in weight. Etiologically, it is important to state that the patient had smoked considerably and indulged freely in alcoholic beverages. The examination showed a markedly enlarged liver, extending to about one finger above the navel, and immensely dilated stomach; the latter reached to the symphysis, and showed continuously pronounced peristaltic restlessness. The gastric contents revealed ischochymia and a high acidity: $\text{HCl} + \text{acidity} = 100$. The duodenal bucket, size No. 23 F., did not pass the pylorus. A smaller one, size No. 18, was given. When it was found that the latter had entered the duodenum, the pylorus was stretched by means of the pyloric dilating catheter. Although an operation was considered necessary, the patient was not in good shape to undergo it at this time, on account of the marked symptoms of inanition and the swollen liver.

After the stretching of the pylorus the duodenal pump was applied, and as soon as it passed into the duodenum, feeding through

the latter began. The patient then began to improve. He was free from pain and vomiting, and developed more strength and vitality almost daily.

The liver grew smaller, and on the eighth day of duodenal feeding was almost normal in size. On the tenth day, during the night, the tube slipped into the stomach and failed to reënter the pylorus. As the patient was much stronger now, the operation of gastro-enterostomy was advocated and performed by Dr. Willy Meyer. The patient made a complete recovery and remained well. Here, as is seen from the report, the stretching of the pylorus was of great benefit, allowing the patient to be built up and be in shape to stand the major operation.

CASE II.—Ulcer of the stomach and benign stenosis of the pylorus. Rev. M. J. D. (Table, Case 6), aged about forty years, was suffering for the last three years from recurrent attacks of severe pains two to three hours after meals. There was occasional vomiting. Patient was treated by several physicians and advised to be operated. The examination showed a moderately dilated stomach, the greater curvature extending to about one finger below the navel, a high acidity: $\text{HCl} + \text{acidity} = 100$, with some minute ischochymia. The duodenal bucket, No. 23 F., failed to pass the pylorus, while No. 18 did. The thread showed ulceration of the lesser curvature of the stomach. Duodenal bucket, size No. 18 F., was again given, and the following morning the pyloric dilating catheter introduced over it and the pylorus stretched.

The duodenal pump was then given, duodenal feeding instituted for a period of two weeks, and then the pylorus was regularly stretched by the usual pyloric dilator. The patient made a splendid recovery, being able to eat ordinary food with impunity.

CASE III.—Dilatation of the stomach and pyloric ulcer with pylorospasm. Frank D. (Table, Case 19), aged forty-three years, ropemaker. Habitual user of alcohol for many years. During the last nine years, he complained of distress and burning in the stomach, acid regurgitation, and occasional vomiting after alcoholic excesses. For the past two years his condition had become worse. He complained of pains in his stomach two hours after meals, lasting for two hours or more, frequently accompanied by vomiting of acid contents, which relieved the pain. During the past two years he lost twenty pounds in weight, and was obliged to live on a fluid diet, and was also unable to work. On April 4, 1913, the patient was admitted to the Postgraduate Hospital.

Examination on admission: poorly nourished man; weight eighty-four pounds. Chest negative. Blood and urine negative. Abdomen soft, no tumors; stomach gives splashing sound two fingers below umbilicus. Liver not enlarged.

Examination after test meal showed HCl , 55, and total acidity, 68; no blood. Duodenal bucket given on April 11, 1913, at night

and withdrawn in the morning, showed a yellow bile stain and a well-marked blood stain in the pyloric region.

April 14 to 28. Duodenal alimentation; weight, eighty-six and one-half pounds.

April 30. Duodenal bucket given and withdrawn in the morning, showed well-marked bile stain and no blood stain.

May 6. Pyloric dilator was given and pylorus stretched to 54 F.

May 7. Stomach washed out in the morning in the fasting condition showed no food remnants from the previous day; weight, eighty-eight and a half pounds.

May 13. Pylorus stretched to 55 F.

May 18. On ordinary diet; weight, ninety-two pounds.

In the table, as well as in the cases described, a distinction is made between pylorospasm and benign stenosis of the pylorus. The easiest way to ascertain which of the two conditions is present, is by measuring the pylorus. In pylorospasm No. 50 to 60 F. can be passed through the pylorus, while in real stenosis No. 40 F. is about the largest size that can go through at first.

Indications for stretching of the pylorus:

1. Stretching of the pylorus can be performed with advantage in all cases of pylorospasm, provided there is no fresh active ulcer in the pylorus or its immediate vicinity. If a fresh ulcer in this region is present, as evidenced by the thread test, a course of treatment should first be undertaken toward the cure of the ulcer. As soon as the thread test becomes negative, careful stretching of the pylorus can be undertaken. If, however, the ulcer shows no tendency to heal, or if there are frequent recurrences indicating exacerbations of the ulcerated process, an operation is indicated.

2. Beginning benign stenosis of the pylorus forms a large field for the treatment by stretching with the same exceptions as mentioned in Paragraph 1.

3. Advanced benign strictures of the pylorus, which cannot be operated: either on account of the great underlying danger, like heart lesions, kidney, or liver, complications, advanced old age, or when the patient absolutely refuses surgical intervention, can likewise be subjected to the internal stretching. In this group the usual pyloric dilator frequently fails to pass, while the dilating catheter over the thread is still able to occasionally enter the pylorus.

As already stated in one of my previous papers, the method of stretching of the pylorus is not antagonistic to surgery. It works hand in hand with it. Where one procedure fails or is unfeasible, the other steps in as its helpmate.

LARGE-CELL SPLENOMEGALY (GAUCHER'S DISEASE): A CLINICAL AND PATHOLOGICAL STUDY.

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OWING to the haze which surrounds the conception of medical men in reference to the subject of the Gaucher type of primary splenomegaly, the authors are prompted to make an attempt to show that this specific form of disease has little in common with a promiscuous group of diseases whose chief characteristic is an enlargement of the spleen. The subject has been still further confused by a recent article appearing in *Surgery, Gynecology, and Obstetrics*, March, 1913, by L. B. Wilson, who reports three cases of primary splenomegaly, Gaucher type, for which splenectomy had been performed at St. Mary's Hospital, Rochester, Minnesota. In the literature which he has considered for the preparation of his article, he assumes as authentic cases many of those belonging to the promiscuous group of splenomegalies to which we have just referred, and which writers who have given much time to an intimate study of this disease have justly eliminated. The reasons for their elimination have already been fully considered in the publications of Marchand, Schlagenhauser, Risel, and others. We can see no clinical or pathological factors which might have justified Wilson in restoring to the list of proved cases of the Gaucher type those in which the verdict against their genuineness has been so unanimous.

There are varying conditions which are attended by splenomegaly. Some of these are plasmodial infections, syphilis, tuberculosis, amyloid disease, rickets, circulatory disturbances in the portal system, blood diseases (including the leukemias), Hodgkin's disease, and a large group, to which the French have particularly called attention, of associated hepatic cirrhoses of a hypertrophic type, with splenic enlargements. Unfortunately to many of these, and particularly to the group of splenic anemias, the term "primary splenomegaly" has been applied. We deem it desirable, therefore, to isolate from this group one form, whose picture is so distinctive clinically, and whose pathological process is so unique, as to merit an individual name. We would therefore suggest that this affection should be called Gaucher's disease, so as to avoid the use of the term "splenomegaly," which is only one of the features of the

disease, but which has occasioned much of the confusion to which we have alluded above.

DEFINITION. The characteristic features of Gaucher's disease are its incidence in childhood, its frequent presence in other members of the family of the same generation, a progressive increase in the size of the spleen which often reaches colossal dimensions, followed by a similar huge enlargement of the liver, a characteristic brownish-yellow discoloration of the skin, usually restricted to the face, neck, and hands, a peculiar yellowish, wedge-shaped thickening of the conjunctivæ commonly seen on both sides of the cornea, and the prolonged and chronic course of the disease, which does not materially disturb the health of the individual. After the disease has been present for a considerable time there is a definite tendency to hemorrhages, especially appearing as epistaxis, bleeding from the gums, and ecchymoses in the skin following the slightest trauma. The positive finding in the blood, even in the early stage of the disease, is a definite leukopenia. The erythrocytes, however, show no definite change either in number, form, size, or hemoglobin content until the disease has existed for a long time, when an anemia of the chlorotic type makes its appearance. The anemia is rarely pronounced at any stage. The disease is not accompanied by palpable enlargements of the superficial lymph nodes. There is no jaundice and ascites is exceptional. The disease has none of the characteristics of malignancy, and usually is terminated by some intercurrent affection.

The pathological feature of the disease is the presence in the spleen, liver, lymph nodes, and bone-marrow of distinctive large cells, with characteristic cytoplasm and small nuclei. The enlargement of the spleen and liver is due to the presence of these cells in enormous number. In well-established cases all of these organs contain pigment giving the reaction for iron. Whereas the nature and origin of these cells are still moot questions, the histological picture is uniformly characteristic and pertains to no other form of disease.

ANALYSIS OF INDIVIDUAL SYMPTOMS. While there are no individual symptoms which are pathognomonic of this disease, we believe that a definite association of certain symptoms is sufficient to enable one to clinically diagnosticate its presence. It was this association of symptoms which enabled one of us to make the diagnosis clinically in two cases, which was subsequently confirmed by pathological examination. A detailed analysis of these clinical factors is justified owing to their importance. We shall, however, confine ourselves strictly to such cases as have been proved by histological examination of the tissues obtained either by autopsy or by splenectomy. We purposely shall not consider the cases occurring in brothers and sisters presenting the identical clinical picture as the affected member of the family, because absolute scientific confirmation is lacking.

The cases established under these conditions are: (I) Gaucher,¹ 1882; (II) Collier,² 1895; (III) Picou and Ramond,³ 1896; (IV) Bovaird,⁴ 1900; (V) Brill, Mandlebaum and Libman,⁵ 1904; (VI) Schlagenhauser,⁶ 1907; (VII) von Herczel,⁷ 1907; (VIII) Marchand,⁸ 1907; (IX) Brill, Mandlebaum and Libman,⁹ 1909; (X) De Jong and van Heukelom,¹⁰ 1910; (XI) Mandlebaum,¹¹ 1912; (XII) Wilson,¹² 1913; (XIII) Downes,¹³ 1913; (XIV) Erdmann.¹⁴

ONSET. In the large majority of cases the beginning of the disease cannot be determined, because it starts insidiously and is unattended by any subjective symptoms which might attract the attention either of the parent or the affected individual. After the disease has existed for some time and has given rise to a splenic enlargement, which in some patients may produce symptoms of discomfort or slight pain, it first begins to attract attention; in others, in the course of a physical examination for some other condition, which may have no relation to the disease itself, a splenic hypertrophy is discovered.

AGE. As a rule the disease begins in early life. Among the fourteen proved cases the age at which the disease was detected is as follows: Case I at seven years; Case II at two years; Case III at twenty-eight years; Case IV at three years; Case V at nineteen years; Case VI at five years; Case VII at thirty-three years; Case VIII at twenty-four years; Case IX at twenty-one years; Case X at seven and a half years; Case XI at three and a half years; Case XII at twelve years; Case XIII at thirteen years; Case XIV at one year. From this it may be seen that the disease appeared before the age of twelve years in the majority of cases and in infancy or early childhood in several instances.

SEX. Females are more frequently affected than males. In the fourteen reported cases the disease occurred in males only twice.

¹ De l'épithélioma primitif de la rate, Paris, 1882.

² Trans. Path. Soc. London, 1895, xlv, 148.

³ Bull. Soc. anat. de Paris, 1895, lxx, 531; Archiv. de méd. expér. et d'anat. path., 1896, viii, 168.

⁴ AMER. JOUR. MED. SCI., 1900, cxx, 377.

⁵ Proc. New York Path. Soc., 1904, iv, 143; AMER. JOUR. MED. SCI., 1905, cxxix, 491.

⁶ Verhandl. d. deutsch. path. Gesellsch., 1907, x, 77; Virchow's Archiv. f. path. Anat., 1907, clxxxvii, 125.

⁷ Wien. klin. Woch., 1907, xx, 127.

⁸ Münch. med. Woch., 1907, liv, 1102.

⁹ AMER. JOUR. MED. SCI., 1909, cxxxvii, 849.

¹⁰ Beitr. z. path. Anat. u. z. allg. Path., 1910, xlviii, 598.

¹¹ Jour. Exp. Med., 1912, xvi, 797.

¹² Surg., Gyn., and Obst., 1913, xvi, 240. An examination of the slides which were kindly sent to us by Dr. Wilson revealed the undisputed existence of the disease in only one of his three reported cases. This conclusion was arrived at after careful and critical study. Our reasons for excluding two of his cases will be referred to later in the article.

¹³ Med. Record, 1913, lxxxiii, 697.

¹⁴ In a recent communication before the New York Surgical Society, J. F. Erdmann presented a spleen which he had removed from a child, aged three years and four months. A portion of the spleen was kindly furnished to us. It shows the presence of the disease in an early stage. An article reporting this case will be published later in the AMER. JOUR. MED. SCI.

FAMILIAL OCCURRENCE. The disease often affects more than one child of the family. There seems to be no tendency to hereditary transmission, and in none of the established cases has any parent been affected. If one wishes to include those cases in the family, which from a clinical standpoint have the same symptoms as the individual proved case, then the familial character has been noted seven times. The authors who have mentioned such cases are Collier; Bovaird; Brill, Mandlebaum, and Libman; Schlagenhauser; De Jong and van Heukelom; Mandlebaum; Erdmann.¹⁵

ENLARGEMENT OF SPLEEN. The splenic hypertrophy is one of the important features of the disease. It is slowly progressive, occurs in every case, and gives rise to a distinct protrusion. The amount of abdominal and thoracic protrusion is in direct proportion to the increase in size of the affected organ. While at first the left side of the trunk is decidedly enlarged, with the subsequent increase in size of the liver, the anomalous one-sided protrusion becomes symmetrical. At the latter stage the trunk is definitely barrel-shaped, the lower part of the thorax joining in a distinct curve with the upper part of the abdomen. The time required for the spleen to reach colossal proportions may be many years. The size of the spleen is greater than that in any other disease, not even excepting leukemia. The upper border may be percussed even as high as the fifth rib in the axillary line, and the lower border not infrequently extends below the iliac crest into the pelvis, so that it cannot be felt by abdominal palpation. Anteriorly the rounded edge may be traced by palpation to the region of the umbilicus, where it often curves to the right, and may thus occupy the greater portion of the abdomen. The posterior border may often be felt in a line continued vertically from the angle of the scapula; occasionally it may even be felt along the vertebral column. At the umbilicus a distinct notch is usually felt, whose depth may admit three fingers. In some cases, however, more than one notch may be felt. The surface is usually smooth, even though a considerable amount of perisplenitis be present.

ENLARGEMENT OF LIVER. This seems to develop only after a considerable increase in size of the spleen has taken place. It gives rise to the uniform thoracic and abdominal protrusion referred to above. Its upper border may reach the fourth rib, and its lower border be felt 3 cm. below the umbilicus. Occasionally the splenic enlargement may so overlap the liver that the lower border of the latter can only be felt in the anterior axillary line and posteriorly. The surface is also uniformly smooth.

SKIN. Early in the disease the skin of the face and neck, as well as the hands, presents a peculiar discoloration. It is usually spoken of as a pigmentation,¹⁶ but we prefer to call it a discoloration,

¹⁵ Personal communication.

¹⁶ No histological examinations of the skin affected by this discoloration have as yet been made.

because it is uniform in distribution and intensity, and is limited to the parts of the body exposed to light. In one case only has this discoloration been noted on the abdomen. The color is a peculiar yellowish-brown (ochre). It frequently assumes a deeper shade across the bridge of the nose and around the eyes, and after the disease has existed for a considerable time the discoloration becomes uniformly more intense. Often the skin presents numerous ecchymoses, varying in size and color, because the superficial vessels are particularly susceptible to injury from the slightest trauma. Furuncles assuming a hemorrhagic character have been noted, which on healing have left definite and permanent skin lesions of a dark pigmented nature.

Some authors describe this specific discoloration as a jaundice or a subicteric tint. Our own analyses show an absence of bile in the blood and urine, with an excess, however, of urobilin in both. A tendency to general sweating associated with sudamina has been noted in a few cases.

EYES. Early in the disease a change in the conjunctiva of both eyes may be noted. This manifests itself in a brownish-yellow, wedge-shaped thickening, affecting first the nasal side of each conjunctiva, its base being limited by the cornea. Later on the temporal side also becomes the seat of a similar thickening. The development and growth of these thickenings are very slow. They seem to originate near the corneal margin and extend in the process of growth to the inner and outer canthus respectively. They resemble in some respects the lesion of the conjunctiva known as pinguecula, and may reach dimensions of 3 mm. along the corneal margin and 5 mm. in length. We have never seen a case of the disease in which this peculiar ocular lesion was absent, and therefore again emphasize its diagnostic significance.

HEMORRHAGES. There seems to be a tendency in all of the cases to bleeding from the mucous surfaces. In most of the cases epistaxis is a frequent occurrence; in some cases this is associated with bleeding from the gums, which are often swollen and spongy. Melena and metrorrhagia have been observed. Attention has been called above to the occurrence of hemorrhagic furuncles and numerous ecchymoses in the skin.

BLOOD. An important positive factor is a leukopenia which appears early in the disease and persists throughout. As few as 500 leukocytes to the cubic millimeter have been noted. The average count of all the reported cases is 4600. The differential count, using the average of all the authentic cases, is as follows: Polynuclears, 66; small lymphocytes, 20; large lymphocytes, 13; eosinophiles, 1. In two cases myelocytes were found, 2 per cent. and 1 per cent. respectively. Mast cells were also noted in two cases, 0.8 per cent. and 0.5 per cent. respectively.

It is remarkable that notwithstanding the fact that the disease

involves the entire hemopoietic system, its effect on the blood-forming organs should be attended by so little demonstrable change in the morphological characters of the blood. The number of erythrocytes is not materially diminished until the disease has existed for some years. The red-cell count for quite a long period is close to normal. Later in the disease a diminution slowly takes place. In the advanced cases the average of all the reported counts is 3,700,000. As high as 6,000,000 red cells have been noted in one case. There seems to be a greater reduction in the hemoglobin content than in the number of the red cells, giving rise to a low color index, and therefore of a mild anemia of the chlorotic type. The appearance of the patient does not even suggest an intense degree of anemia, because the skin of the majority of patients does not show an inordinate amount of pallor, nor do their mucous membranes.

There is little if any change in the contour, shape, or size of the red cells. The color may be slightly paler than normal. In only two of the cases have nucleated forms been observed; in these a solitary normoblast was seen in each. Megaloblasts have never been noted. The large specific type of cell, the so-called "endothelial cell," whose presence in all the hemopoietic organs characterizes the disease, is never found in the peripheral circulation. The hemoglobin shows a reduction before the red cells suffer any marked decrease. Its average in all the cases reported is 65 per cent. As high as 92 per cent. and as low as 35 per cent. have been observed.

LYMPH NODES. The superficial lymph nodes of the body are not usually palpable. Where careful search is instituted, occasionally a few solitary lymph nodes in the axilla and in the groin may be felt as small, hard, pea-sized bodies.

ABSENCE OF JAUNDICE AND ASCITES. We have already directed attention to the peculiar brownish-yellow discoloration of the skin of those parts of the body which are exposed to light. This discoloration has been called jaundice by some writers. We insist that this is a misnomer, because bile pigment has not been found in the blood or urine. Ascites is almost invariably absent, even though the disease has existed for twenty-five years or more. In only one case has it been reported.

SYMPTOMS OCCASIONALLY MANIFEST. After the spleen and liver have grown to a large size a few patients complain of abdominal pain, chiefly referable to the region of the spleen. This pain is not constant. It may be absent for many months before it is complained of again. During the period of pain, tenderness over parts of the spleen may be elicited. This would seem to be occasioned by the presence of local areas of perisplenitis. Pain and tenderness over the liver are only exceptionally present. The weight of the spleen and liver gives rise in a few patients to a sense of dragging discomfort in the abdomen. It is remarkable that not-

withstanding the colossal size of the spleen and liver, there is very little complaint in the majority of the patients referable to these organs.

Very late in the existence of the disease, only after many years, some patients direct attention to pain in the lower ends of the femur and tibia, and still later to pain and tenderness in the muscles of the thigh and calf. Bone tenderness over the sternum and tibia is absent.

A remarkable feature of this disease, to which we have already drawn attention, is the preservation of the feelings of comparative comfort and well-being which dominate the patient. As a rule, patients do not feel depressed, nor are their mental activities diminished.¹⁷

EMACIATION. Most of the advanced cases present a loss of adiposity. The appearance of the patient, with the tremendously enlarged abdomen and the emaciated frame, makes a striking picture. In one of our cases, a female adult, there was a total body weight of 89 pounds.

DURATION AND TERMINATION. The disease is essentially chronic; its course is slow and progressive. Schlagenhauser's patient lived for thirty-six years after the disease was detected. The average duration of all the authentic reported cases where death has not resulted from splenectomy is 19.3 years. The disease is usually terminated by some intercurrent affection. A few of the reported causes of death are tuberculosis, pleurisy, and pericarditis. Operative procedure (splenectomy) has occasioned three deaths. Another case died as the result of an accident causing a fracture of the skull and laceration of the brain.

PATHOGENESIS. Much speculation has been indulged in to explain the nature and origin of this disease. When first described by Gaucher its nature gave rise to considerable discussion, and it was considered by some to be a form of malignant disease. Later writers, taking into consideration its clinical course, its long duration, as well as its histological features, have justly disproved this assumption. Various theories have been offered, such as the influence of an endogenous toxin, of an enzyme manufactured by the spleen, infection by protozoa, tubercle bacilli, and the like. No evidence has ever been presented which might substantiate any of these as causative factors. While it is true that a tropical form of splenomegaly, known as kala-azar, exists

¹⁷ One of the patients now under observation, in whom the disease is known to have existed for at least twenty-four years, presenting a gigantic spleen and liver, which together almost completely occupy the entire abdominal cavity, is still able to attend to her household duties and social functions, and though forty-four years of age, still indulges in the summer in sea-baths, swimming, and tennis. This is one of a family in which four cases have occurred. The existence of the disease in two of these cases was confirmed by autopsy. We have purposely added this case in a footnote, so as to adhere to the plan expressed above, to include in our paper only the cases which have been proved histologically.

in which protozoa have been found, a thorough search for similar organisms has always failed. In the present state of our knowledge the confession must be made that we know nothing definite of the pathogenesis of this disease.

DIAGNOSIS. While the diagnosis of the disease in its early stage is well-nigh impossible, owing to the absence of associative symptoms, the fact that more than one member of the family may be afflicted with varying degrees of combined splenic and hepatic enlargements ought to suggest the possibility of its existence. When the disease has sufficiently developed, so as to give rise to a distinctly large spleen, even though but one member of a family be affected, the diagnosis, while difficult, may possibly be made. The factors which might enable one at this stage to determine the existence of the disease are the large spleen, a beginning hepatic enlargement, the conjunctival lesion, and the absence of anemia, jaundice, and ascites. Blood examinations must always be made, so as to exclude the possibility of a leukemia.

When the disease is fully developed the diagnosis ought to be possible in the majority of cases. The enormous enlargement of the spleen and liver; the brownish-yellow discoloration (non-icteric) of the skin; the conjunctival thickening; the long duration of the disease; its predilection for females; its familial occurrence; the feeling of comfort and ease, notwithstanding the tremendous protrusion of the lower thorax and abdomen; the tendency to hemorrhage, manifested by epistaxis and bleeding from the gums; the ecchymoses in the skin; the persistent leukopenia; the mild degree of chlorotic anemia without changes in the red cells; the absence of jaundice and ascites; the absence of palpable lymph nodes, make a symptom complex which differentiates this disease from the groups called splenic anemia and Banti's disease, with which groups it is most likely to be confounded.

While it is true that splenic anemia and Gaucher's disease have much in common, yet we believe, contrary to Hutchison,¹⁸ that they are distinct and can readily be separated. The features common to both are the splenic enlargement, the chronicity of the affection, the hemorrhagic tendency, the absence of leukocytosis, and the anemia of the chlorotic type. The differential factors are the relatively shorter duration of the disease in splenic anemia; the pallor of the skin, which toward the end becomes distinctly jaundiced; the more pronounced type of the anemia, which occurs early and is a prominent factor in the disease; the feeling of distress and illness; the tendency to hemorrhages of a more generalized type, as expressed by frequent attacks of hematemesis as well as melena; the relatively smaller size of the spleen; the markedly smaller size of the liver; the absence of the conjunctival

¹⁸ A System of Medicine, Allbutt and Rolleston, 1909, v, 759.

lesion, and the presence of ascites. These factors are so distinctive that in a large majority of cases the differential diagnosis between Gaucher's disease and splenic anemia may be established.

It was the recognition of these differential factors which enabled one of us (Brill),¹⁹ De Jong and van Heukelom, and Reuben²⁰ to diagnosticate the presence of Gaucher's disease during life, which diagnosis was subsequently confirmed by histological examination in each instance.

The disease may be confounded with chronic splenomegalic acholuric jaundice, which likewise is a familial form of disease, and occurs in infancy and early childhood, sometimes hereditary, and is associated with anemia, with considerable enlargement of the spleen, and a moderate enlargement of the liver. The distinctive blood changes, such as fragility of the red blood cells, normoblastic and megaloblastic crises, and leukocytosis, would differentiate this from Gaucher's disease.

Hanot's disease is likewise characterized by its chronic course as well as by a large liver and spleen. Jaundice in this disease is an early symptom, and exists continuously in varying degrees of intensity. At any time during the course of the disease an icterus gravis may occur. The urine usually contains bile. Its course is generally attended by fever, which is rarely or ever present in Gaucher's disease. The hepatic and splenic enlargements are moderate as compared with the hypertrophy of these organs in Gaucher's disease. Leukocytosis is usually a prominent feature.

It would appear unnecessary to mention in this connection the possibility of mistaking leukemia, Hodgkin's disease, and pernicious anemia for Gaucher's disease. The characteristic blood picture and the enlargement of the lymph nodes in leukemia would immediately differentiate it, although the possibility of a stage of remission in leukemia with an approximately normal blood-count might be met with, when a differential diagnosis would be established with greater difficulty. Even under such conditions the marked pallor of the skin, the enlarged superficial lymph nodes, and the absence of leukopenia would suggest some other condition than Gaucher's disease.

The only form of Hodgkin's disease which would admit of the possibility of error in diagnosis is the splenomegalic form without enlargement of the lymph nodes. Such a form, however, is still a moot subject of discussion. The usual form of Hodgkin's disease, while it may present some enlargement of the spleen, is commonly associated with periods of fever and with greatly enlarged lymph nodes. A combined splenic and hepatic enlargement of colossal size does not occur in Hodgkin's disease.

¹⁹ AMER. JOUR. MED. SCI., 1901, cxxi, 377.

²⁰ Amer. Jour. Dis. Child., 1912, iii, 28.

The characteristic high color index, the definite changes in size and shape of the red-blood cells, together with the nucleated forms, the extreme degree of anemia, the color of the skin, the preservation of the adiposity, are sufficient factors in establishing the diagnosis of pernicious anemia, even though a moderate degree of splenic enlargement be present.

French authors, particularly Chauffard, Lereboullet, Gilbert and Fournier, and Gilbert, have described under the terms metaspleno-megalic hypertrophic biliary cirrhosis, prespleno-megalic hypertrophic biliary cirrhosis, hyperspleno-megalic hypertrophic biliary cirrhosis, and a special juvenile type with great splenic enlargement, a medley of diseases whose existence has seldom been met with in any other country than France. The clinical history and pathological features of these forms are so involved, both in obscurity and chaos, and the characters which would entitle them to clinical entities are so meager and ill-defined, that it is possible some of these forms may have been examples of unrecognized Banti's disease or Gaucher's disease.

PATHOLOGY. The description of the pathology herewith presented is based upon the investigation and study of the material obtained post mortem in three cases, and upon the spleens obtained after splenectomy in two other cases, representing in stage of development, the early, the intermediate, and the late periods of the disease.²¹

The organs involved in Gaucher's disease are the spleen, liver, lymph nodes, and bone-marrow, all of which show the presence of peculiar large cells and a variable amount of iron-containing pigment. The large cells are characteristic and present the following features. They are usually round or oval in shape, but when seen in large compressed masses may assume a polygonal outline. The average measurement is from 20μ to 40μ in diameter, and a cell may contain from one to four or more nuclei of relatively small size. When smears are made from the freshly cut organ (Fig. 1), cells of hugh size may frequently be found.²² The cytoplasm stains faintly with acid dyes and often presents a streaked and wrinkled appearance, but with high magnification a granular character may be noted. Some of the cells show vacuoles, probably the result of phagocytosis. Degenerative forms are not present excepting in cases of long duration, but in the liver the cells may be so fused that their individual outlines are not easily recognized. The nuclei are small, round, deeply staining, or, occasionally, somewhat larger irregular bodies. Rarely do the nuclei show atypical mitotic changes. Whereas the cells are quite unlike any found in other

²¹ The ages of the patients from whom this material was obtained were three years, four and a half years, twenty-eight years, thirty-four years, and thirty-seven years.

²² A cell of this type from the spleen measured 71.7μ by 100μ , and contained thirteen nuclei.

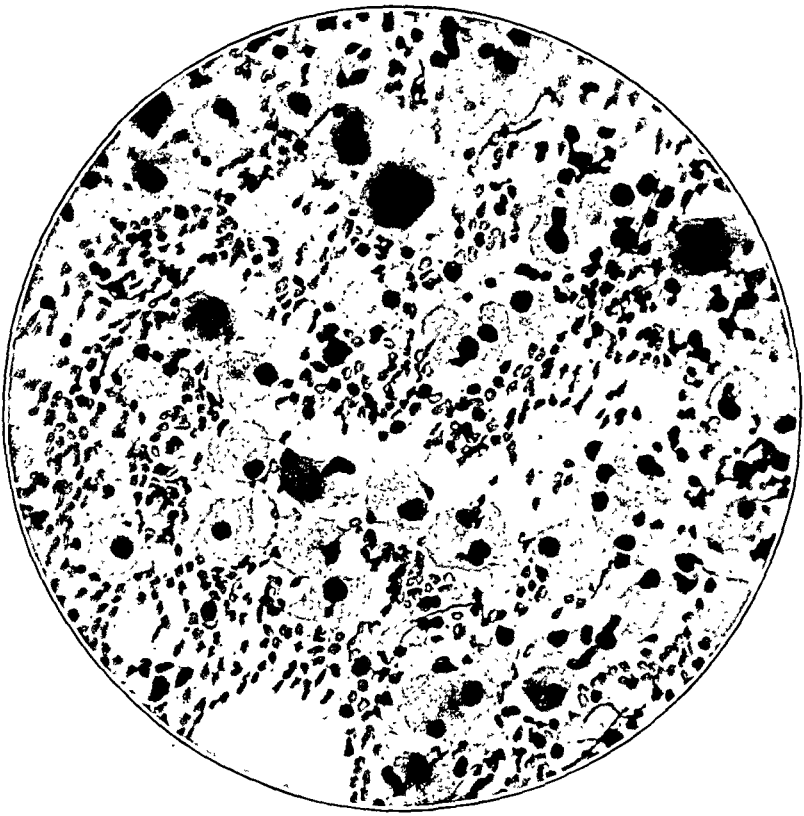


FIG. 1.—Smear from fresh surface of spleen. The size of the large cells as compared with the red-blood cells is readily appreciated. $\times 300$

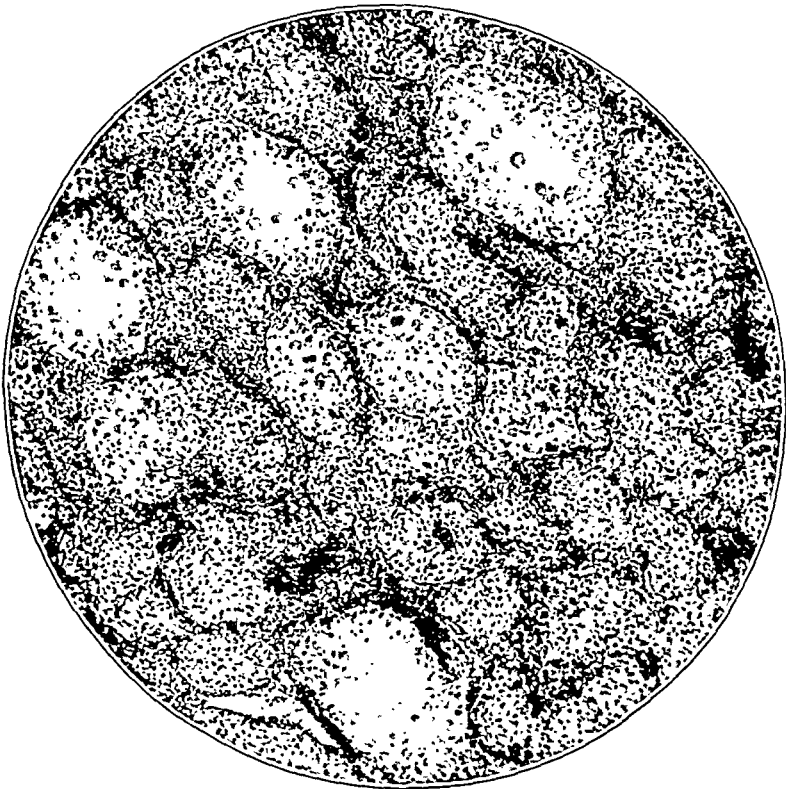


FIG. 2.—Section of spleen showing dilated venous sinuses filled with blood cells (not visible with low power) and large cells. Remainder of field composed of alveoli completely filled with large cells and separated by normal pulp cells. $\times 80$.

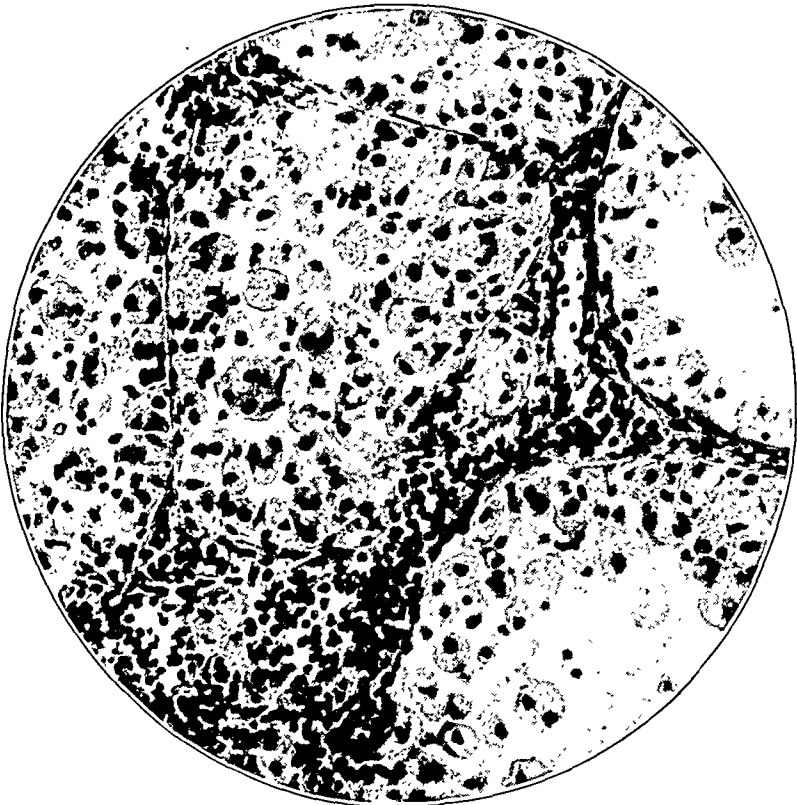


FIG. 3.—Section of spleen. On the right are segments of two sinuses containing large cells and red-blood cells. Connective-tissue septa between the alveoli are seen above and on the left. $\times 300$.

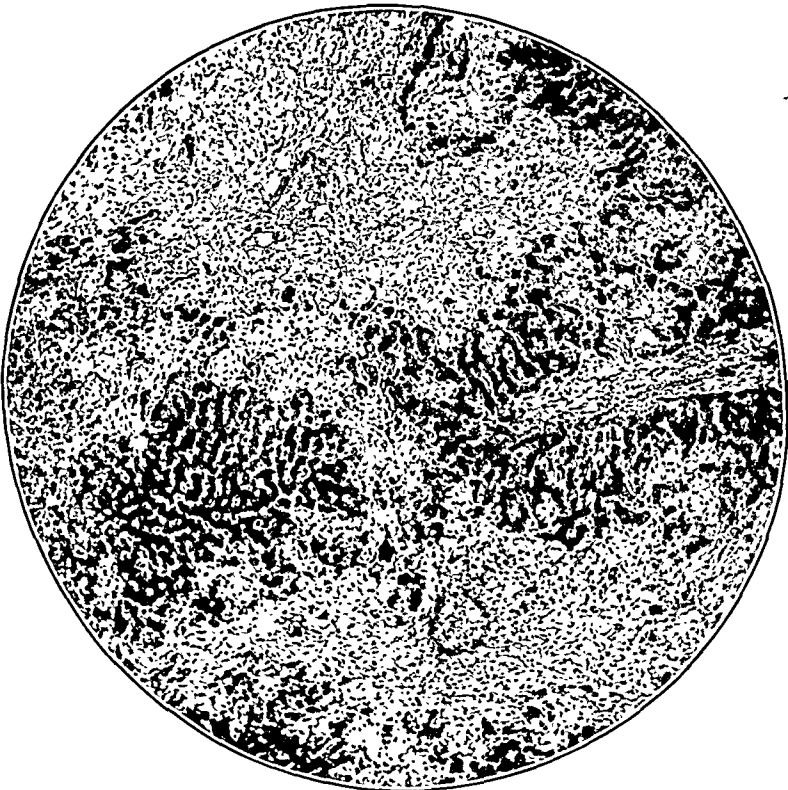


FIG. 4.—Section of liver showing the large amount of interlobular connective tissue. The large cells cannot be differentiated with this power. $\times 80$.

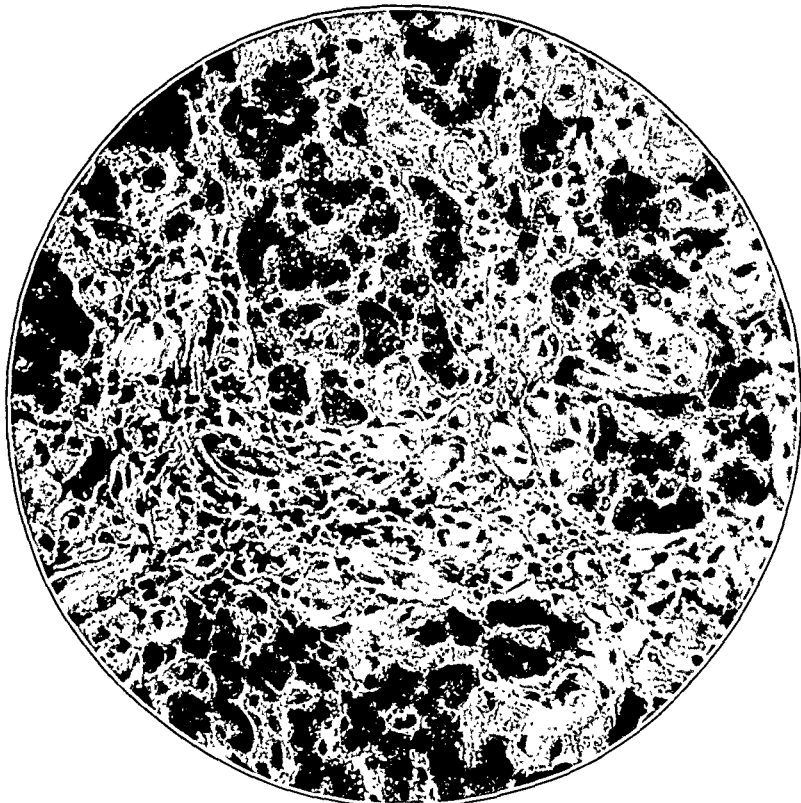


FIG. 5.—Section of liver showing large cells in the meshes of the connective tissue and in the sinusoids. The large cells are compressed and their outlines somewhat obscure. $\times 300$.

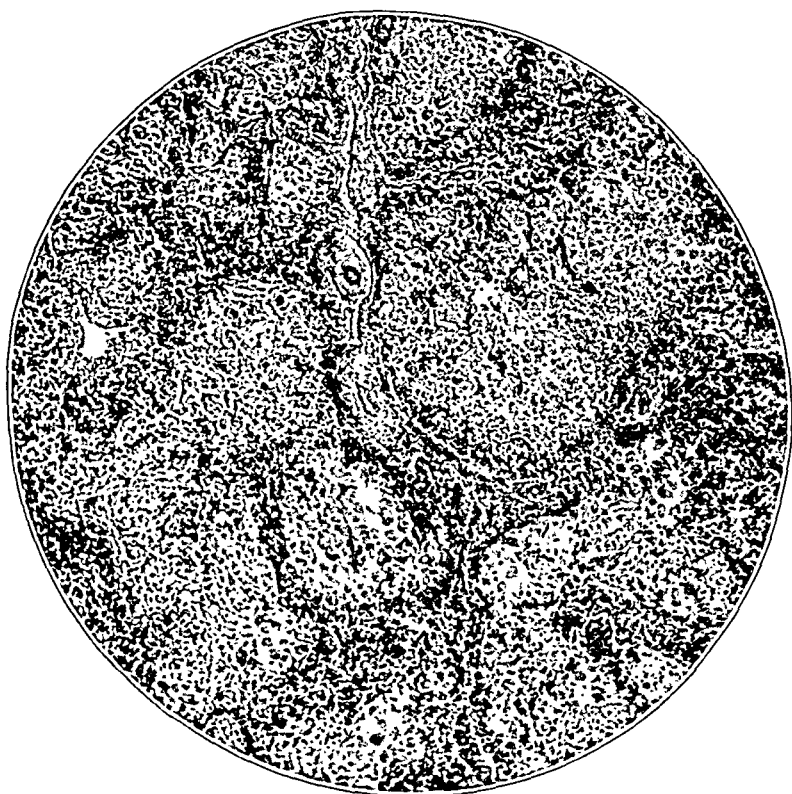


FIG. 6.—Section of retroperitoneal lymph node. The large cells form distinct cellular masses, between which are seen strands of normal lymphoid cells. $\times 80$.



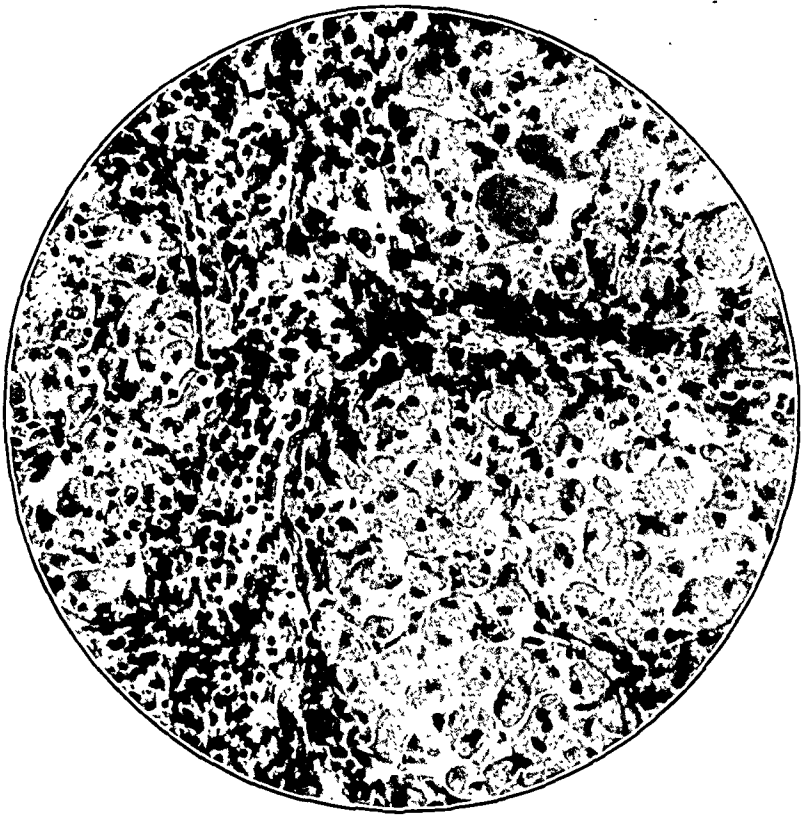


FIG. 7.—Section of same node, showing lymph sinuses filled with large cells whose outlines are clearly distinguished. $\times 300$.



FIG. 8.—Section of bone-marrow from the tibia, showing compressed and distorted large cells. On the left and below are small groups of normal marrow cells. $\times 300$.

pathological processes, one might compare them with atypical, swollen, and desquamated endothelial cells.

SPLEEN. This organ always retains the shape and general appearance of a spleen. The surface is perfectly smooth excepting in cases of long duration, when the capsule may be markedly thickened and rough, and show scattered areas of perisplenitis, as well as localized depressions due to infarctions. The color varies from brownish pink to brownish red. The cut surface is usually brownish red and often mottled with white or grayish streaks. The Malpighian bodies are not visible, nor can the trabeculæ be recognized. Minute hemorrhagic dots are frequently seen, and the infarcts when present are often surrounded by hemorrhagic zones. The splenic vein in adult cases may show slight sclerosis; it is frequently of high size.

The spleen varies in size and weight according to the duration of the disease. In one of our cases it measured 45 x 25 x 13 cm. and weighed 7400 grams (14 pounds 13 ounces), one-sixth of the entire body weight. The average weight in thirteen authentic cases (including the one of only 490 grams obtained from a child) was 3600 grams (7.2 pounds).

Microscopic examination shows that the normal splenic structure is replaced by large, round, or irregularly shaped, alveolar spaces, whose walls are formed by delicate connective-tissue fibres, distinctly lined by endothelium. These spaces represent the greatly dilated venous sinuses of the organ (Fig. 2). In all these spaces the characteristic large cells are seen, some lying free, others attached to the endothelium. Many of the sinuses also contain red blood cells. Sinuses are also seen, presenting the same general appearance and filled with large cells, but without definite endothelium (Fig. 3). A few normal pulp cells are usually found between the sinuses, also capillaries of normal appearance. Reticulum fibres cannot be detected within the sinuses. In most cases the follicles are few in number, and with the exception of a slight thickening of the walls of the central artery in long-standing cases, show no changes. In early cases, however, the follicles may be of enormous size. Scattered throughout the pulp are isolated groups of the typical large cells, and some of these large cells are usually seen between the lymphoid cells at the peripheral portions of the follicles. The germinal centres of the follicles in early cases show atypical lymphoid cells without mitotic changes, also large nucleated cells (phagocytes) containing Flemming bodies. Early cases may also show large cells resembling megakaryocytes, containing fused masses of deeply staining nuclear matter. Large hemorrhagic areas are not uncommon in long-standing cases, and pigment is invariably present. This is seen between the connective-tissue fibers of the trabeculæ, within the endothelial cells of the capillaries, and in many of the typical large cells. The pigment

granules are brown or brownish yellow in color, and show the usual iron reaction. The early cases, however, show little or no pigment. In cases of long duration areas of degeneration may be found, but the contours of the large cells may still be recognized, as a rule. In two cases, Schlagenhauser's and Erdmann's, areas of tuberculosis were observed. These we believe are only incidental and have no bearing or relationship to the diseased process.²³

LIVER. In young individuals the surface is smooth and glistening; its color is a light yellowish pink. On section the same color is noted and the lobules are but faintly indicated. In the older cases the surface may be slightly uneven, owing to localized areas of perihepatitis with irregular thickening of the capsule. The color in these cases assumes a darker hue of brownish red. On section the parenchyma swells above the cut surface; its color varies from a brownish pink to a brownish red. A few grayish streaks and markings are often noted, but they bear no relation to the usual lobular outlines. Occasionally fine hemorrhagic points are seen. The size of the liver is invariably increased, and is in direct proportion to the duration of the disease. In one of our cases the weight of the liver was 4800 grams (10 pounds). The average in all adult cases where the weight of the liver was noted (five in number) was 3450 grams (7.2 pounds).

The noteworthy feature of the liver, microscopically, is the enormous amount of interlobular connective tissue, which gives the usual picture of a fibrosis when examined with the low power (Fig. 4). A more critical examination, however, shows that a great number of cells, identical in type with those found in the spleen, are situated in the meshes of the connective tissue. Many of these cells have lost the typical appearance, and individual cells cannot always be differentiated. They frequently appear as flattened or compressed and fused masses (Fig. 5). In the sinusoids, however, isolated large cells are found. These cells usually are well-preserved, but they are not directly connected with the reticulum fibrils which form a delicate net-work between the columns of liver cells. In the advanced cases most of the large cells in the sinusoids are situated near the peripheral portions of the lobules.

²³ At the 1912 meeting of the German Pathological Society, W. H. Schultze reported a case of diabetes, with marked lipoidemia, in a man aged twenty-seven years. The spleen, which was only slightly hypertrophied, contained large cells, in which Schultze found a distinct lipid substance. No large cells were found, however, in any of the other organs. On account of the similarity of the cells to those found in Gaucher's disease, he calls attention to the possible occurrence of a lipid substance in the latter. No fresh material being available, our observations to establish this fact could only be made on a portion of spleen fixed in formalin. We succeeded in obtaining a faint stain with Nile blue, but the results with the Fischler, Smith-Dietrich, and Ciacio methods were not corroborative. A final decision as to the presence of a lipid in the cells in Gaucher's disease should not be made until the various methods have been employed on frozen sections of fresh unfixed material, for Bell (*Anatomical Record*, 1910, iv, 199) has shown that formalin solutions often have a solvent action on lipoids, and the staining methods may give negative results in consequence of such fixation.

The individual liver cells are not apparently affected by the presence of the large cells, nor are any changes noted in them as the result of compression by the interlobular connective tissue. Occasionally the liver cells show a somewhat coarsely granular appearance, and in old cases minute fat droplets have been seen. None of the large cells in the liver appear to have phagocytic properties. In the early stages of the disease iron-containing pigment is absent, but in the more advanced stages it is always found, situated in the capsule as well as in the neighborhood of the smaller bloodvessels, but not in the large cells. The bile-ducts are not affected and appear normal, and no changes are present in the intralobular veins or in the branches of the hepatic artery.

In Schlagenhauser's case numerous miliary tubercles were found in both lobes of the liver. We do not believe that they have any direct relationship to the disease.

LYMPH NODES. In noteworthy contrast to the usual absence of enlarged superficial lymph nodes, those in the thorax and abdomen are always increased in size. The mesenteric, retroperitoneal, and iliac lymph nodes, also the nodes at the hilus of the liver and the spleen, and those in the region of the pancreas, are enlarged in early cases. They measure from 0.5 cm. to 2. cm. in diameter, and are usually soft and friable. The color is brownish gray or reddish gray or a bright red, or the surface may be pale and the central parts deep red. The bronchial lymph nodes are also enlarged and present a similar color.

In advanced cases the abdominal and thoracic lymph nodes are also increased in size, but to a relatively less degree than in children. In our own cases none of the nodes exceeded 2 cm. in diameter. The color varies from yellow or ochre to dark red, and in very advanced cases the nodes may be brownish black. The yellowish nodes may show hemorrhagic markings on section.

Microscopic examination in the advanced cases shows the presence of the typical large cells, extensive fibrous changes, a large amount of pigment, and a diminution or entire absence of lymph-adenoid tissue. The large cells are frequently present in such enormous numbers that the picture of a glandular organ is commonly absent. The connective-tissue framework is intact, however, and an occasional follicle or a small remnant of lymphoid tissue may still be preserved here and there (Fig. 6). Notwithstanding the presence of large cells in such abundance, the individual cell bodies are clearly and distinctly outlined, and fusion of cells is rarely seen in the lymph nodes. The large cells are found also in the lymph sinuses (Fig. 7). The capsule is often greatly thickened and the trabeculae very prominent, giving the appearance of a fibrosis. The large cells appear to have a definite relationship to the reticulum and to the endothelium of the lymph sinuses. The pigment is dark brown in color, crystalline or amorphous in char-

acter, and always gives the reaction for iron. It is distributed throughout the node, but is most abundant in the sinuses under the capsule and along the trabeculæ. Pigment crystals are often found in the large cells, giving evidence of their phagocytic properties.

The lymph nodes in the early cases show variations in the degree of involvement. Some groups present an involvement which may be as far advanced as in the adult cases; other nodes may show the lesion in an earlier stage. In our last case, a boy, aged four and a half years, the iliac, mesenteric, retroperitoneal nodes, and those at the hilus of the liver, presented an older type of lesion than the bronchial and pancreatic nodes or the nodes near the splenic vein. The general picture in the advanced lesion in children is identical with that described in adult cases, but the capsule and trabeculæ are less prominent, and pigment is absent. The follicles may show great hypertrophy of the germinal centres with much cellular activity, as evidenced by active mitosis in the lymphocytes. Eosinophile myelocytes may be found in these nodes in considerable number.

The nodes presenting an early type of lesion may appear quite normal with low magnification. The typical large cells are seen, however, if a more critical examination be made, and they can be found in the lymph sinuses and here and there between the pulp cells. The follicles are quite prominent, and in the germinal centres phagocytic cells containing remnants of red-blood cells and pigment may be noted. In our case a small amount of pigment was found in all of the nodes showing the early type lesion, but in the nodes about the splenic vein it was very prominent. It appeared as rounded granules of yellow or brownish color and was always situated in large cells which bore a striking resemblance to the typical large cells of the disease. Remnants of red-blood cells were also present in these phagocytic cells, side by side with the pigment granules. A close relation of reticulum and large cells could be seen in these nodes. Eosinophile and neutrophile myelocytes were present, also a few polymorphonuclear cells with eosin granulations.

BONE-MARROW. The lesion in the bone-marrow was first noted by us in 1904, twenty-two years after Gaucher's first description of the disease. The color of the bone-marrow is always red, and small white or yellowish areas may be present. The consistency, as a rule, is soft. The typical large cells are found either singly or in groups, and no characteristic variation in the degree of involvement between early and advanced cases is apparent. At times the large cells may be seen in extensive groups, and in such situations considerable distortion of the cells may result from compression (Fig. 8). Reticulum fibers are present between the cells, and a close relationship between the two exists. Some of the large cells show vacuoles, but no distinct phagocytes are seen. Pigment

is present in small amount, but only in cases of many years' duration, and is found in the vicinity of the larger bloodvessels. Small areas of normal lymphoid tissue may be discovered in the early cases. Those portions of the marrow not involved show normal cells, including myelocytes of all types, eosinophile and neutrophile leukocytes, normoblasts and megakaryocytes.

OTHER ORGANS. In many of the cases a considerable degree of hypertrophy has been found in the lymph-adenoid tissue of the lower ileum and cecum, also marked pigmentation in the muscle fibers of the intestine. In Schlagenhauser's case fine pigment granules of a yellow color were seen in the muscular tissue of the uterus, and marked perivascular pigmentation was noted in several normal organs, including the salivary glands. The thigh muscles in Marchand's case were the seat of hemorrhages and pigmentation, with an active new formation of striated fibers.

Although the large cells typical of the disease are found only in the hemopoietic system, it is noteworthy to mention that Risel²⁴ reports finding some of these cells in a connective-tissue septum of the thyroid gland in Marchand's case. Inasmuch as a small collection of lymphoid cells was seen nearby, one may reasonably assume that the latter represented misplaced lymph-adenoid tissue in which the large cells had their origin.

TREATMENT. This paper would be incomplete if no reference were made to the treatment of the disease. Before splenectomy came into vogue as a remedial measure, attempts at cure had been made by drugs, chief among which was arsenic in its various forms administered by mouth and hypodermically, and local injections into the spleen of methylene blue and pyoktanin. None of these agents seemed to have any influence upon the progress of the disease, nor did they produce any amelioration in the condition of the patient. The only effect of the x-rays applied to spleen and bones was to temporarily reduce somewhat the size of the spleen without arresting the disease.

It is too early to give judgment upon the value of splenectomy. While the blood seems to regain some of its normal elements, such as the increase in the number of red and white cells and the amount of hemoglobin, we cannot say how permanent this change may be. Of the 8 splenectomies performed among these 14 cases, 3 died as a result of the operation. Of the remaining 5, no report has been made, so far as we know, by Picou and Ramond or by von Herczel in reference to the subsequent history of their cases. In De Jong and van Heukelom's case, however, the liver continued to enlarge. The cases of Downes and Erdmann have so recently been operated that the signs of improvement which at present are manifest may be only temporary. It would seem to us that a disease which is

²⁴ Beitr. z. path. Anat. u. z. allg. Path., 1909, xlv, 241.

not confined to the spleen, but involves all the organs of the hemopoietic system, could not be materially stayed in its progress by the removal of but one member of this system. However the future must decide. Inasmuch as more improvement has resulted from splenectomy than from any other measure it is our duty to recommend this operation and to insist that it be performed as soon as the disease is suspected.

DISCUSSION. Were it not for the fact that an extensive literature pertaining to the subject of Gaucher's disease has been steadily accumulating, containing reports of alleged cases based on meager observation, insufficient symptomatology, and uncorroborated by histological examination of any tissue, the authors would have deemed their work concluded without further discussion. But many of these cases which have found a position in this literature ought to be, once and for all, removed. While the original reporters of some of these have not diagnosticated their individual cases as belonging to the Gaucher type, subsequent commentators have included them in the list, chiefly because they were of familial type and had large spleens and anemia.

Among those most frequently cited are the following: Weichselbaum,²⁵ Harris and Herzog,²⁶ Rolleston,²⁷ Borissowa,²⁸ Springthorpe and Stirling,²⁹ Stengel,³⁰ Umber,³¹ O'Malley and O'Malley,³² Cowan,³³ Rettig,³⁴ and Plehn.³⁵ In their original contributions, Borissowa, Stengel, Rettig, and Plehn described their cases as belonging to the category of Gaucher's disease.

Borissowa's case has occasioned considerable study and discussion, and has been analyzed by Marchand, Askanazy, Schlagenhauer, Risel, and De Jong and von Heukelom. These authors are not unanimous in their opinions as to the exact nature of her case, but they are agreed that it does not belong to the Gaucher type. The cells are much smaller, the cytoplasm has entirely different characteristics, and the nuclei are much larger than in Gaucher's disease. Naegeli,³⁶ who examined the blood, called attention to the presence of megalocytes, megaloblasts, and the high color index, as well as marked leukocytosis and 3 per cent. of myelocytes.

Through the kindness of Dr. Stengel we had the opportunity in 1905 of studying the sections in his case, and concluded that they

²⁵ Virchow's Arch. f. path. Anat., 1881, lxxv, 562.

²⁶ Ann. Surg., 1901, xxxiv, 111.

²⁷ Clin. Jour., 1902, xix, 401.

²⁸ Virchow's Arch. f. path. Anat., 1903, clxxii, 108.

²⁹ Lancet, London, 1904, ii, 1013.

³⁰ AMER. JOUR. MED. SCI., 1904, cxxviii, 497.

³¹ Zeitsch. f. klin. Med., 1904, lv, 289.

³² AMER. JOUR. MED. SCI., 1905, cxxix, 996.

³³ Quart. Jour. Med., 1908, i, 11.

³⁴ Berlin. klin. Woch., 1909, xvi, 2046.

³⁵ Deutsch. med. Woch., 1909, xxxv, 1749.

³⁶ Blutkrankheiten und Blutdiagnostik, 1908, 401.

presented no histological evidences in common with our own. This conclusion was also reached by Ledingham,³⁷ who says that Stengel's case cannot be included "in the category either of Banti's disease or the Gaucher type of splenomegaly."

Rettig's one case (the daughter) showed, in addition to a moderate enlargement of the spleen and liver, and a discoloration of the skin, the presence of enlarged cervical, axillary, and inguinal lymph nodes, and a decided leukocytosis, the latter features being uncommon to Gaucher's disease. His other case (the father) presented a similar picture, though the lymph nodes were not enlarged. Plehn's cases represent a disease occurring in two generations, father, son, and daughter. Both Rettig's and Plehn's cases have been diagnosticated on purely clinical grounds. They have many points of similarity with the clinical picture of the disease, and we shall await with interest subsequent communications which may substantiate their diagnoses.

Weichselbaum's case lacks all clinical data, and its histology is very meager. If a conclusion could be reached from his facts, one might suspect that his case represented an endothelial sarcoma, an opinion which Risel also entertains.

Harris and Herzog's first case was subjected to a splenectomy. From the histological examination one is not justified in including it in this group. Marchand, Schlagenhauser, and Risel, independently, have expressed doubts as to its genuineness.

Rolleston at no time intimated that his case was one of Gaucher's disease. In his clinical lecture on splenic anemia he incidentally discusses the subject of Gaucher's disease, without even hinting that either of the two cases therein presented were anything else than splenic anemia.

Springthorpe and Stirling's cases belong to one family and appear in two generations. On account of the familial occurrence alone, some authors have included them under the group of Gaucher's disease. Their clinical data are insufficient for this conclusion. Splenectomy was performed upon two of them, but the reports of the histological examination are lacking in detail and insufficient to justify the diagnosis.

In the case reported by O'Malley and O'Malley the spleen diminished 10 cm. in size while under observation, the liver also became reduced in size, ascites was present, and a moderate grade of leukocytosis was noted. The patient died after splenectomy. The liver showed atrophic cirrhosis without "unusual endothelial proliferation;" the spleen had none of the characteristics of Gaucher's disease.

Umber stated positively that his first case was one representing an early stage of Banti's disease. On this account we cannot

³⁷ A System of Medicine, Allbutt and Rolleston, 1909, v, 773.

understand how any writer could have included it under Gaucher's disease. Having read his clinical history and the report of the histological findings in the spleen and liver, we can find no evidence to disprove Umber's own diagnosis of Banti's disease. Umber's second case, a seventeen-year-old boy, who had sixty-four liters of ascitic fluid removed during a period of four months, finally recovered. Umber states in his paper that his original diagnosis of Banti's disease was incorrect, and that the disease was probably a thrombotic process in the branches of the portal vein following scarlet fever.

Cowan was unable to classify his cases, stating that they resembled cases of splenic anemia in infancy. A perusal of his communication does not support in our minds the conclusion of other writers who have placed them in the group of Gaucher's disease.

We regret to see that Wilson, who is one of the latest contributors to the subject of Gaucher's disease, has included in his three cases two which admit of the most serious doubt. The author himself asserts in his article that one of his cases is quite identical with Stengel's case. He describes in the third a colloid degeneration as a later process of the disease. Wilson's first case (No. 8869) is a typical example of Gaucher's disease. The second case (No. 9315), like Stengel's, shows an enormous amount of connective tissue, mostly arranged in bands encircling the venous sinuses. The large cells seen in the sinuses show branching forms lacking the more or less rounded contours seen in other cases, and the nuclei appear relatively large, though we admit that this appearance may be due to shrinkage. Giant cells resembling the Langhans type are present in large numbers. These are seen in the sinuses and also between the lymphoid cells. The resemblance to a tuberculous lesion is most striking, even though distinct tubercles are not seen. In none of the other cases have giant cells of this variety been encountered in the sinuses. In a few of the cases isolated multinuclear cells described as "giant cells" have been observed, but there is no recorded case excepting that of Stengel in which giant cells of the Langhans type have been found in such profusion. For these reasons we do not believe this case to belong to the category of Gaucher's disease. Wilson's third case (No. 58,571) has no resemblance whatever to any lesion described as characteristic of Gaucher's disease. The sections show enormous spaces (sinuses) filled with a homogeneous, faintly granular material, giving the impression of a circulatory disturbance with stasis and resulting exudation. It is true that in a few situations, particularly in small sinuses under the capsule, large desquamated endothelial cells are found, but this is not uncommon in many forms of splenic hypertrophy due to various causes.

Having given an exposition of the constituent factors of Gaucher's disease, there still remains the consideration of the views of various

authors as to the origin of the characteristic large cells and the nature of the pathological process. Briefly summarized these are as follows: Gaucher believed that the disease represented a primary epithelioma of the spleen. Collier concluded it to be an endothelioma. The Morbid Growths Committee who examined his slides denied the sarcomatous nature of the process. Picou and Ramond thought the disease represented a primary epithelioma, non-malignant at the beginning, which was converted later into a malignant process, which subsequently involved the lymph nodes. Cornil, who discussed this case, expressed the opinion that it was a primary hypertrophy of the spleen with proliferation of the reticulum.

Bovaird regarded the disease as "a hyperplasia of the spleen, characterized by an unusual development of endothelial cells and the transformation of a considerable part of the organ into dense connective tissue." He likewise considered the lesion in the lymph nodes and liver to be an endothelial hyperplasia, confined in the liver to the lymph spaces in the perilobular connective tissue. He suggests the likelihood of "the action of some systemic poison affecting several members of a family."

Brill, Mandlebaum and Libman thought that the large cells arose from endothelium or normal reticulum in the hemopoietic apparatus, and suggested a peculiar susceptibility of these structures to some unknown toxic agent. They stated that tuberculosis, when found in these cases, must be considered as a superimposed process.

Schlagenhauser stated that the large cells could be readily differentiated from the endothelial cells and did not arise from them. He considered the process to be a systemic disease of the lymphatic-hemopoietic apparatus, with proliferation of the reticular structures, affecting the spleen primarily, then the regional and other lymph nodes, and finally the liver and bone-marrow. For a time he thought that the tuberculous lesions were secondary, but finally decided that some toxin, probably of a tuberculous nature, but without other manifestations of true tuberculosis, was the most likely etiological factor.

Von Herczel considered the spleen to be the seat of an inflammatory process or a new growth. The histological examination was made by Krompecher, who confessed his inability to explain the complicated picture. Risel subsequently examined the slides and found the typical picture of Gaucher's disease. This diagnosis was accepted by Krompecher.

Marchand was of the opinion that the cells might have their origin either from reticulum or endothelium, and that they contained some unknown substance of a peculiar homogeneous, amyloid nature, with the properties of some form of semi-solid hyaline material. Risel, after a more detailed study of the material in Marchand's case, concludes that while there is no positive proof that

the cells arise from reticulum, and no transitional stages between reticulum and cells can be observed, nevertheless he believes the reticulum must be their seat of origin. He also states it is his belief that in the lymph nodes the cells may arise from the endothelium of the lymph sinuses, late in the course of the disease, as well as from the reticulum within the follicles. He admits that the presence of the cells in the venous sinuses of the spleen is difficult of explanation, assuming that they originate in the reticulum. He concedes that the cells are carried to the capillaries of the liver through the portal vein, but he acknowledges his inability to explain their presence in the connective-tissue spaces of Glisson's capsule.

De Jong and van Heukelom concluded that the cells arise from proliferated reticulum, but could not deny the possibility of an endothelial origin. They believe that the cells have the power of multiplying, because they found peculiar cells undergoing direct cell division in the spleen, and because the liver continued to enlarge after splenectomy in their case.

Mandlebaum thought that the large cells might be derived from large lymphocytes or reticulum cells in the germinal centres of the follicles, and described the phagocytic cells found there. The large cells are carried through the portal vein to the liver, and he believes that their destruction in this organ causes an irritation leading to the production of the connective-tissue process.

Downes calls attention to the extensive, uniform, diffuse, endothelial hyperplasia, and says that the cells "resemble those seen in the so-called 'large-celled hyperplasia' of lymph sinus endothelium."

Wilson considers the process to be a "primary endothelial proliferation with a secondary proliferation of fibrous connective tissue, and ultimately a degeneration of the endothelium with contraction of the connective tissue." He concludes that the large cells are "much more likely to have arisen from the endothelium than from the reticulum."

From the above opinions it may be seen that while all are agreed as to the histological features of the lesion, the source and nature of the cells are still wrapped in mystery. We recognize the fact that neither an origin from reticulum alone nor endothelium alone will explain the pathological features in all the organs. Neither will the theory of an origin from large lymphocytes or reticulum cells in the germinal centres of the follicles explain all of the lesions. It has been shown by Rössle and Yoshida³⁸ that no differentiation between reticulum and endothelium, especially in lymph nodes, can be made. Therefore it is possible that in the lymph nodes at least the large cells may arise from both of these structures.³⁹

³⁸ Beitr. z. path. Anat. u. z. allg. Path., 1909, xlv, 110.

³⁹ A full discussion of the various factors concerned in the attempted explanation of the pathogenesis of this disease is to be found in the original articles of Schlagenhauser, Risel, De Jong and van Heukelom, and Mandlebaum.

We believe that the disease starts simultaneously in the spleen, bone-marrow, and lymph nodes. In the last, however, it may appear somewhat later or be slower in development, an assumption which finds its support in the fact that we have found in a very early case, a child aged four and one-half years, the process in some of the nodes to be far less advanced than in the spleen and marrow.

If in this communication we have succeeded in giving a place in nosology to what appears to us to be a distinctive clinical and pathological entity we shall be satisfied. This satisfaction would be the more complete and our object more fully accomplished, could we hope that in the future all the cases which lack the distinctive features of the disease would be excluded from the literature.

NOTE.—Since the above was written, with the kind permission of Wilson, the slides of his three cases were submitted to Marchand for an opinion. Marchand writes that Wilson's first case is a typical splenomegaly of the Gaucher type. He agrees that the second case is one of tuberculosis, even though tubercle bacilli could not be demonstrated in the sections or by animal inoculation. The third case, he says, looks like a lymphangioma, although small collections of cells, seen under the capsule, resemble somewhat those found in Gaucher's disease. A study of these cells in the fresh state would be necessary, however, before giving a final opinion as to the nature of the lesion.

ADDENDUM.—An opportunity to examine fresh unfixed material for the presence of lipoid substance has been afforded since this paper has gone to press. Through the courtesy of Dr. E. P. Bernstein we have just obtained from the pathological laboratory of the Lebanon Hospital a piece of spleen removed at operation from a case of Gaucher's disease. Tests with the polariscope, as well as examination of frozen sections stained with Nile blue and Sudan III are negative, thus indicating the entire absence of neutral fat, cholesterin, and cholesterin esters from the large cells in this disease. Chemical studies for the purpose of extracting lipoids from the spleen are now in progress.

METALLIC POISONS AND THE NERVOUS SYSTEM.¹

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THIS subject is presented not so much because of being anything especially out of the ordinary, for many of the things which will be mentioned may have been known to some, but one fact that I feel sure is, as is well stated by Gowers, the commonplace of all knowledge, that which we can least afford to despise or to disregard.

In a recent number of *Everybody's Magazine* appears a popular (if not also somewhat exaggerated) article entitled "The Lead Menace," by Gordon Thayer, in which the author endeavors to show the importance of the passage of the Occupational Disease Bill, introduced in several State legislatures at the instance of the

¹ Read before the Medical Society of the City and County of Denver, Colorado, April 1, 1913.

American Association for "Labor Legislation" for the protection of workers exposed to lead perils. In studying the many cases in the literature the great variety of nervous manifestations is found to be quite remarkable.

With these ideas in mind supplying a feeling of justification in doing so, I will first briefly present three cases, showing the effects of lead intoxication, one of arsenic and one probably of mercury, upon the nervous system, and later draw from the literature a few observations concerning this subject.

CASE I.—C. W. S., aged fifty-three years, painter by occupation, was first seen August 15, 1908. He came to Colorado two weeks previously on account of rheumatism. The family history was negative. Other than the ordinary diseases of childhood, he had jaundice at nineteen, rheumatoid pains at twenty-four, and malaria at thirty-nine years. Four years before he had a severe attack of colic, with vomiting and dysentery. Gonorrheal infection was admitted and syphilis denied. Used alcohol occasionally, and at times to excess. Five months prior, following the taking of a cathartic, a lot of clear blood and clotted blood was passed, also some blood in the urine. This has occurred since. The patient complained of increasing weakness in the arms and shoulders, with considerable pain. There had been no absolute loss of power. Otherwise the health had been good. On examination he appeared anemic; was 5 feet 8½ inches in height, and weighed 136 pounds. The muscles of the shoulders, arms, and forearms were symmetrically wasted, and the eminences of the hands diminished. Power was much diminished and the right arm could only with great difficulty be brought to a horizontal position. Dynamometer (inner scale, Tiemann): R., 120; L., 180. He is right-handed. Tremor was absent in the hands, but a fibrillary twitching was evident in the deltoid and pectoral muscles. All coördinate movements were well performed, and the deep reflexes were all present and equal. All extensor muscles of the arm and forearm, as well as the supraspinati and infraspinati, showed a diminished faradic response, while prompt contractions were obtained in the flexors of the arm and forearm and the anterior shoulder muscles. The tongue was coated and the breath foul. A bluish-black line was to be seen at the margins of the gums in the upper and lower jaws.

The case was regarded as a muscular atrophy, and due to chronic lead intoxication. The absence of the wrist-drop or extensor paralysis was noteworthy, but the usual predilection of the extensors was evident in the diminished faradic responses. Of interest also was the occurrence of pain, for which he had been advised to come to this city, with the belief that it was rheumatic. Whether or not the bleeding from the bowels and kidneys was a result of the high vascular tension so common to lead could only be inferred. The usual eliminative treatment, with massage and stimulation, by

increasing doses of strychnine and iron to overcome the anemia, resulted in sufficient improvement to permit of resuming work in



FIG. 1.—Case I, showing atrophy of the spinati.

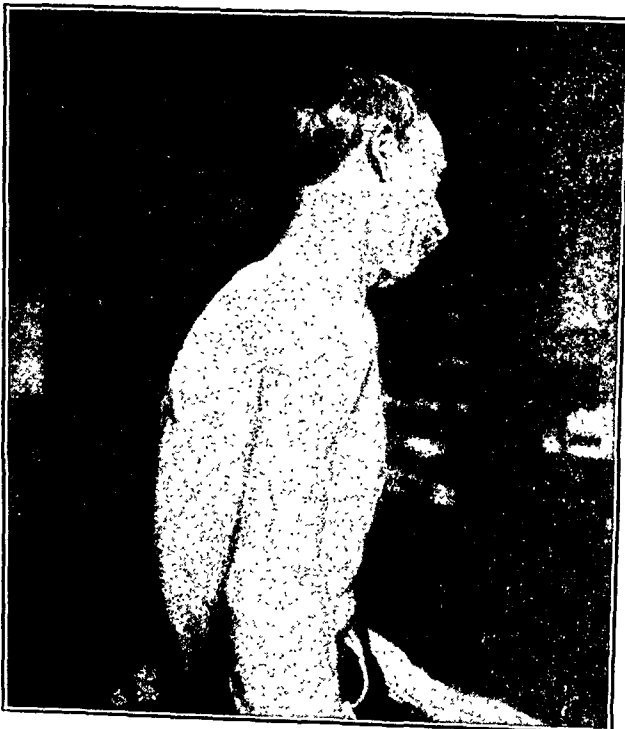


FIG. 2.—Case I, showing atrophy of arm including the deltoid.

a few months as a wood finisher, avoiding lead, but a complete recovery of the atrophy was hardly to be expected.

CASE II.—T. N. D., aged sixty-five years, painter by occupation, was referred in January, 1910, by Dr. Packard, on account of pain in the left arm and in the fingers, accompanied by numbness in the thumb and forefinger of the left hand and pain in the right leg. A year previously he experienced pain in the left arm and wrist, and believes it was weaker at that time. The family history contained nothing of importance, and other than that he had chills at twelve years, he had not been ill until three years previously, when he was treated for lead poisoning and had colic for about a year. Drank moderately, but never to excess; denied venereal infection.

On examination he appeared fairly well-preserved and of fair color. There were no paralyses and no wasting; muscular power was good. Dynamometer: R., 215; L., 180. He is right-handed. Facial action was present and equal. The tongue was protruded mesially. The margins of the gums of the lower jaw, and to some extent of the upper, showed a distinct bluish-black line.

The right knee-jerk failed in response even on reinforcement, while the left was present. The forearm reflexes of the left side were not as prompt as on the right. Both plantar reflexes were flexor. The right abdominals were less active than the left. Electrical reactions were normal. No sensory disturbance could be made out, other than slight hyperalgesia in the left forearm. Ocular motion was normal, and there was no nystagmus. Pupils were equal and responded actively to light and distance. The right fundus appeared normal, while the left appeared atrophic and presented some small hemorrhagic spots in the retina.

A neuritis, with perineural hyperemia and attributable to plumbism, was believed to be present, and the ordinary treatment was followed by prompt recovery. The absence of the right knee-jerk may have been attributed to the same cause, being distinctly unilateral, with a strong probability of being correct.

While the following case presents one of the more common effects of lead intoxication but also unilateral in type, there were associated circumstances which were misleading:

CASE III.—The patient was a housewife, aged forty-eight years, and had a negative family history, with the exception of a brother who died of tuberculosis, and a sister who became paralyzed at fifty-two years. Had no illness of consequence until two years previously, when a complete hysterectomy was done. About five months after operation, numbness of the right arm was noticed; this was accompanied by weakness, and she would drop things from the hands. There was no pain and she seemed to recover completely.

She was first seen January 27, 1913, and about ten weeks pre-

viously had fallen, striking and injuring the right knee, for which a cast was applied for three weeks. The patient was about on crutches for four or five weeks, when the right arm became numb, and loss of power was noticed. Otherwise she was in good health.

Examination revealed an anemic-appearing woman of good development, who presented a loss of power of the extensors of the arm, forearm, and hand, giving rise to the classic wrist-drop. The deltoid was unaffected and the supinator was likewise free. A fine lateral tremor of the fingers of both hands was present, but no tremor of the tongue. Grasp as indicated by dynamometer: R., 20; L., 180. She was right-handed.

There was total inability to extend the arm, and the hand likewise could not be extended. No sensory loss could be made out. The deep reflexes were normally present and equal, except the forearm extensors and the triceps jerk, which were much diminished.

There was a slight lateral nystagmus on extreme rotation of the eyes. Otherwise the external ocular muscular movement was normal. The fundi showed no change and the pupils were equal and responsive. Fields of vision were not contracted. Hemoglobin, 80 per cent. (Dare).

At the dental margins of several teeth a bluish-black line was to be seen, while it was absent over many others.

While one would think of a crutch paralysis in this case, the fact that the extensors alone, and especially the exception of the supinator, served to exclude this cause. Again, the first attack of paralysis and numbness, from which she had recovered, antedated the use of crutches.

Inquiry revealed the fact that prior to the paralysis there had been considerable painting done throughout the home, quite a lot of white lead was used, and the patient herself had done a great deal of the painting, and had frequently handled the lead.

The eliminative course of treatment, followed by stimulation and massage, and the exercising of the muscles by electricity, was followed by prompt return of power.

The following case presented an unusual effect of what appeared to be arsenical intoxication:

CASE IV.—N. A., aged thirty-four years, a brother of a physician, was referred by Dr. Melville Black, December 22, 1911, on account of optic atrophy. Family and previous history negative. Venereal infection was denied, and alcohol as well. A great deal of Paris green had been handled in combating insects on potato vines. The patient was in direct contact with it, and, at times, his eyes would smart, while at other times, the backs of his hands would blister after handling it. After breathing the dust he would occasionally have a "funny feeling in the nostrils."

On January 15, 1911, double vision was noted which continued

a few months, and then disappeared. About two months before examination the vision of the left eye began to blur, and three weeks previously the right eye, especially on the temporal side, became affected, and the vision of both eyes have progressively failed since. Other than the failure in vision he was perfectly well. No tremor was noted. The patella and Achilles reflexes were absent, and there was some slight unsteadiness in gait and station. All other reflexes were about normal and equal. Sensation was present in all forms.

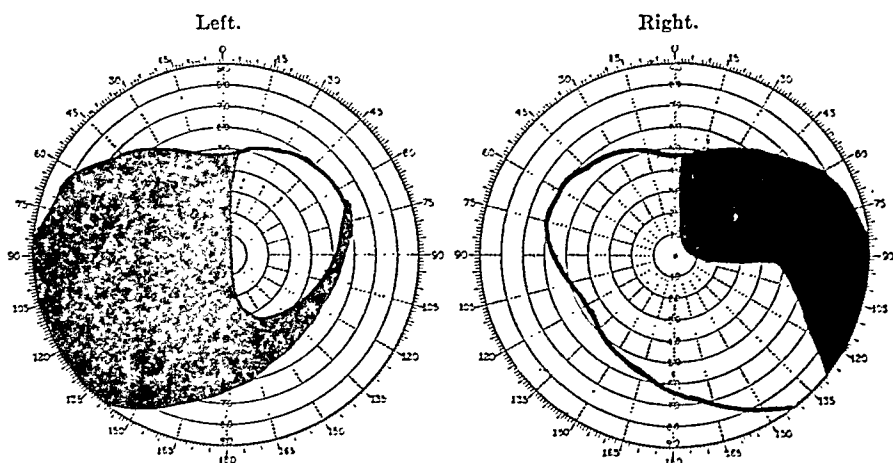


FIG. 3.—Case IV. December 22, 1911. o. d. v., $\frac{20}{30}$; o. s. v., finger in nasal field.

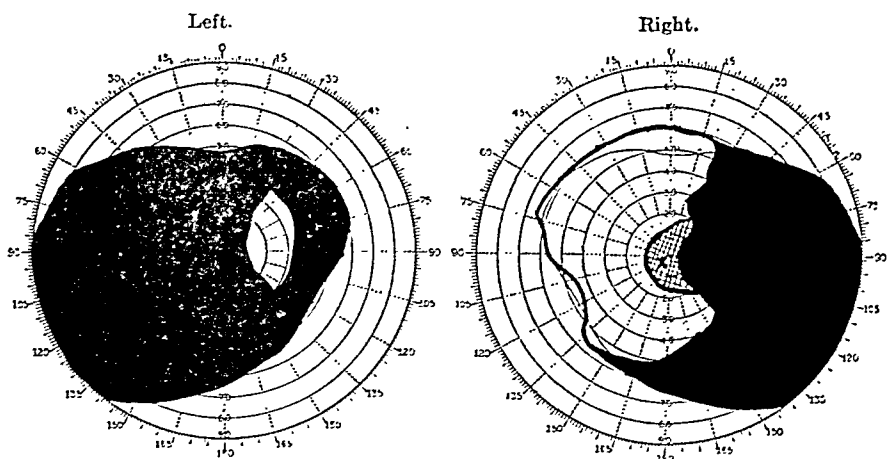


FIG. 4.—Case IV. January 26, 1912. o. d. v., eccentric, too weak to estimate; o. s. v., almost nil. Relative scotoma at x.

March 8, 1912. Dr. Hillkowitz reported the blood reaction as showing a Wassermann positive (Bauer-Hecht). The eyes showed no muscular impairment. Pupils were equal and responded to light and distance, the left less promptly than the right. Vision: R., eccentric, with central relative scotoma; L., almost *nil*. Fields

(see chart) showed a segmental blindness on the right and a small area on the left. Fundi: R., retina appeared normal—disk, marginal degeneration on the temporal side; lamina cribrosa quite marked; L., marked attenuation of vessels, disk distinctly atrophic, greenish white in cast; marginal degeneration on the temporal side. Hearing: $\frac{2}{2}$ in either ear. Aërial conduction greater than bone. A subsequent report from this case indicated the rapid progression of the blindness, which was then quite complete. Later, in view of the bilateral temporal blindness, the sphenoid was explored with

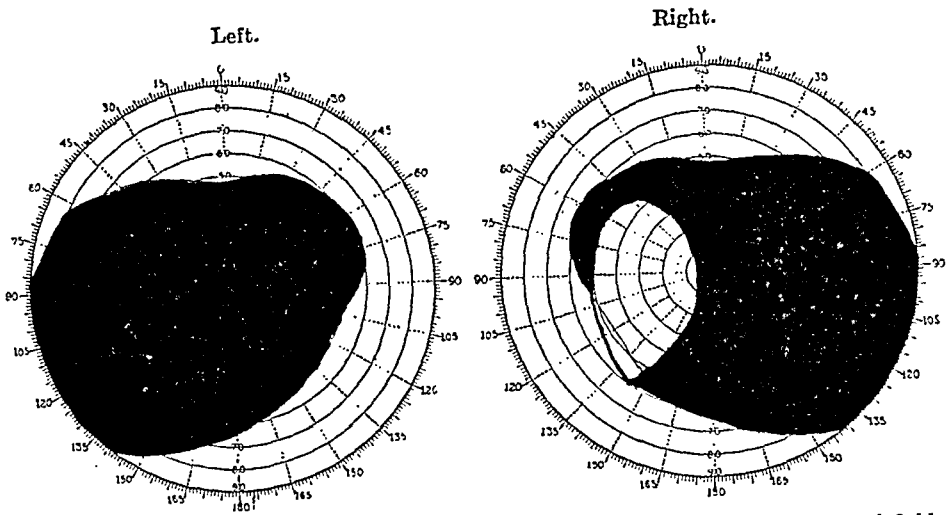


FIG. 5.—Case IV. February 28, 1912. o. d. v., eccentric; o. s. v., shadows in nasal field.

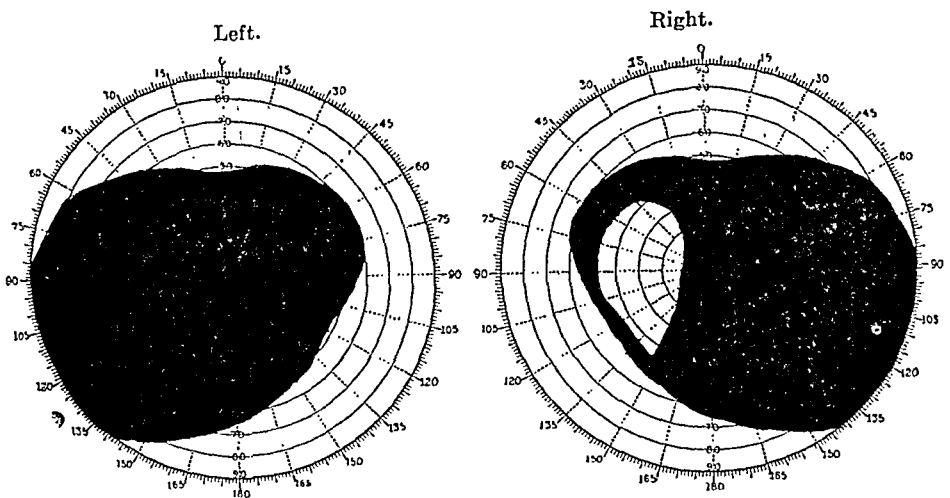


FIG. 6.—Case IV. March 12, 1912.

negative findings, and a skiagram showed no enlargement of the sella turcica nor evidence of pituitary growth. Here we have an unusual effect of arsenic, and I think we are justified in the conclusion that it was due to this metal, rather than to syphilis, tabes, or general paralysis for the following reasons: (1) A negative

history of venereal infection (Wassermann reaction is of questionable value in metallic poisonings); (2) direct exposure to arsenic, with history of what was undoubtedly arsenical dermatitis; (3) rapid progression of degeneration without neuritis; (4) segmentation of visual field not distinctly quadrantic, rather than concentric diminution; (5) retention of pupillary response to light; (6) the absence of subjective or objective sensory disturbance.

CASE V.—W. C., aged forty-six years, a refiner of concentrates. Family history negative. He had been treated for various symptoms, but his history of specific infection was open to question.

In 1901 he began to notice numbness in the soles of both feet; this disappeared under iodide of potassium. Then followed dull, aching pains in the calves of the legs. Just prior to the onset he had been engaged in roasting mercury amalgam and the room was filled with the fumes of the mercury. There had been no girdle sense and no urinary difficulty. There was but little unsteadiness in gait, and no ataxia could be made out in the arms. The knee-jerks were absent on both sides, as was also the ankle-jerk. No tremor was to be seen in the tongue, and but slight tremor in the hands. No change in tactile, thermic, pain, or other senses was noted. The pupils were equal, and responsive to light as well as distance. There was no muscular deviation. Vision was $\frac{2}{20}$ in either eye. Disks were both normal. This case was believed to be a mercurial neuritis, and this view was strengthened by the fact that on several occasions he was given mercury because of suspected tabes or syphilis, and each time the neuritis became notably aggravated.

RARE CLINICAL MANIFESTATIONS. The foregoing cases indicate the variability not only in the effects of the metallic poisons upon nerve structures, but carry at the same time the suggestion of an increased susceptibility in some individuals to their action. It is indeed remarkable what a variety of nervous disturbances have been found to be attributable to lead, and it is safe to presume there are many in which this cause has been overlooked.

Aside from the gastro-intestinal symptoms, high blood-pressure, and the more common extensor paralysis as a result of peripheral nerve lesion, there are affected at times, cranial nerves, giving rise to isolated paralyses, such, for example, as the cases of laryngeal paresis reported by O. Séifert,² who cites three cases resulting from lead poisoning. In the first case there was paresis of the arytenoideus proprius in a joiner, aged nineteen years, who had just recovered from lead colic. The second case, a varnisher, who had repeatedly suffered from lead colic, and was affected with saturnine nephritis, which resulted in edema. On laryngoscopical examination the mucous membrane over both arytenoid cartilages appeared

² Berlin klin. Woch. No. 35. Abs. Periscope, Jour. Nerv. and Ment. Dis., 1884, p. 694.

edematous; the vocal cords even in deep respiration remained nearly stationary, the left vocal cord approximating the median line a trifle more than the right one. In phonation the vocal cords approached each other, but failed to make their normal vibrations. The edematous parts were scarified, and after the reduction of the edema the hoarseness completely disappeared. The left vocal cord, however, remained nearer the median line on deep respiration. After death from uremia, beside other changes, the post-crico-arytenoid muscles were found to have undergone pronounced atrophy. In the third case all the interior laryngeal muscles of the right side were completely paralyzed, lead colic a year previous had been followed by repeated attacks of hoarseness; no pulmonary or lymphatic affections were evident.

Mosny, Dupey-Dutemps and Saint-Girons³ report a blindness of twenty-four hours' duration, occurring after a homonymous hemianopsia for a like period, complicated with a pronounced state of torpor and intellectual weakness, which disappeared with the hemianopsia. The authors believe these should be added to the group of visual disturbances originating in lead paralysis, characterized by the sudden appearance of blindness, with conservation of the pupillary reaction, absence of lesion of the fundus of the eye, and a return of vision in a short time. The optic symptoms are believed to have been due to arterial spasm, localized in the occipital region, as a result of lead intoxication.

In 1880 M. Ernest Gaucher⁴ reported a case of a house painter, who afterward engaged in the manufacture of white lead, who was suddenly seized with lead colic. On recovery he returned to work, but in two days fell unconscious. He presented the typical blue line, the lead constipation, and severe headache. Special senses were normal. Appetite was preserved. No albuminuria. Followed by delirium and vertigo; the cephalalgia continued. Shortly afterward he awakened aphasic and agraphic. Intelligence, sensibility, and motility were completely preserved.

In 1883 John J. Putnam⁵ read a paper referring to the simulating of other diseases to lead poisoning; one case resembled lateral sclerosis: one, the transient forms of poliomyelitis anterior; two others a more diffused form of poliomyelitis, while both were cerebral neuroses.

That a distinct ataxic form of neuritis may occur and also present sensory phenomena was shown in those cases reported by Tedeschi,⁶ who states that pseudotabes of saturnine origin is little known. Three observations are given, showing that in saturnism the ataxia is readily localized in the lower extremities, while in the paralytic

³ Bull. et Mém. de la Soc. Méd. des Hôp., 1911, p. 620.

⁴ La France Médicale, June 26. Abs. Periscope, Jour. Nerv. and Ment. Dis., p. 735.

⁵ Trans. Amer. Neur. Assoc., Jour. Nerv. and Ment. Dis., p. 466.

⁶ Il Tommasi; March, 1911, vi, No. 8, 177 to 183.

and atrophic forms it is the rule that the upper extremities are involved. There were sensory disturbances with two of his cases and none in the third.

The mind may be affected, and the literature is replete with cases showing melancholic, maniacal, confusional, and delirious states. In this regard, Kraepelin⁷ states that the known poisonings are of considerable importance as developing among the occupational diseases. Mercurial poisoning not infrequently occurs in miners, makers of mirrors, and also in conditions associated with anti-luetic cures we find mental difficulties, with marked irritability, timidity, perplexity, confusion, delusion, alarming dreams, and sleeplessness. Upon this ground, also, various forms of excited conditions or a gradual loss of psychic functions may develop—mental weakness and judgment, mental dulness, and loss of will-power. Those observed especially in painters, founders, and type-setters, the encephalopathia saturnina follows the acute course of lead delirium, with marked disturbance of consciousness, delusions, blunting of the consciousness, persecutory ideas, suicidal tendencies, etc.

They may even closely resemble the clinical picture of general paralysis, as the case of Delmas and Barbé,⁸ who presented a patient affected with nervous and mental troubles having their origin in lead poison, and quite similar to those of general paralysis. The diagnosis rests upon the previous occupation, paraplegia, and the slow evolution of the symptoms, while certain symptoms of general paralysis were absent, such as the Argyll-Robertson pupil, absence of lymphocytosis, and a negative Wassermann reaction in blood.

Acute cases are few, according to Cowles,⁹ who considers that painful, disabling affections and arteriosclerosis are in the majority.

ETIOLOGY. It is often difficult to ascertain the source of the poison, and especially since, as not infrequently occurs, very small amounts derived from little suspected sources are found to be responsible. Lewin¹⁰ has seen symptoms of lead poisoning from merely a single shot, which had lodged between the teeth, as a woman was eating an apple. Another like case with optic neuritis and finally a brain affection and death, in which the poisoning was traced to the lead-foil wrapping of snuff, of which the young woman consumed 10 grams per day for months.¹¹

Duckerling¹² found that inhalation is the principal source of trouble. The vapor of lead chloride is continually given up from the tinned articles for some time after removal from the bath.

⁷ *Psychiatrie*, eighth edition, i, 100.

⁸ *Soc. de psych. de Paris, Rev. Neurol.*, 1911, p. 720.

⁹ *Boston Med. and Surg. Jour.*, September 5, 1907.

¹⁰ *Archiv f. klin. Chir.*, Berlin, xciv, No. 4.

¹¹ *E. Stadler, Correspondenz-Blatt f. Schweizer Aerzte*, February 10, xlii, No. 5.

¹² *Jour. Hyg.*, London, September, 1908.

PATHOLOGY. Grave degenerations of the tracts and forms of pseudotabes have been met with in all three forms of metallic intoxications. Likewise, mental diseases have been directly traced to them after excluding other possible causes.

Mosny and Malloizel¹³ summarize 47 cases of lead poisoning, with more or less involvement of the meninges. A latent histological meningitis seems to be almost constant in persons recently intoxicated by lead, and they believe it always accompanies lead colic. It may suggest the clinical picture of general paralysis, but differing in the absence of dementia, and by occasional recovery.

René Vincent¹⁴ states that lumbar punctures systematically done in certain saturnine cases have disclosed the existence of a leukocytosis of the cerebrospinal fluid. This is not constant, is absent in old intoxications, and in the course of peripheral nerve lesions especially, this lymphocytosis, which occurs either independent of nerve symptoms or with the characteristic symptoms of meningitis, is collected under the name of saturnine meningitis, and it is stated that it most often follows immediately in the course of the lead colic.

DIAGNOSIS. The diagnosis of lead paralysis ordinarily presents little difficulty if the characteristic extensor paralysis without sensory symptoms and a bluish or dark line at the margin of the gums is encountered, and especially easy if the occupation is one which has to do with the handling of the metal and with a history of attacks of colicky pain and obstinate constipation.

Where these are not to be obtained and for the early detection of saturnism, Frey¹⁵ offers the following means of detecting characteristic blood changes. The blood is dried, fixed with absolute alcohol, and colored with Loeffler's stain. In a certain number of red cells, the granules are colored blue.

It was previously stated that the Wassermann reaction could not be relied upon in cases of lead poisoning. Field¹⁶ reports that in twelve cases of lead poisoning in which a Wassermann reaction was done it was positive in eight cases and negative in four.

Likewise, Schnitter¹⁷ found four positive Wassermann reactions in sixteen cases of lead poisoning, and three of the four, he states, were free from syphilitic taint.

The elevation of blood-pressure was studied by Vaquez,¹⁸ who believes the variations to be more important than the absolute figure. The rise during paroxysms was 50 to 100 mm.

Arsenical poisoning is more often associated with sensory disturbances than is lead, and a mixed paralysis involving the four extremities is the rule.

¹³ Revue de Méd., June, 1907.

¹⁴ La Méningite Saturnine, Thèse de Paris, 1910, No. 56.

¹⁵ Deutsch. med. Woch., February 7, 1907.

¹⁶ Jour. Amer. Med. Assoc., lviii, No. 22, 1681.

¹⁷ Deutsch. med. Woch., xxxvii, No. 22.

¹⁸ Sem. Méd., 1904, xxiv, No. 48.

Case IV is very unusual, and I have, in the limited literature at my disposal, been so far unable to find an optic nerve atrophy attributable to arsenic. The absence of sensory disturbance, while not usual, would seem in this case to negative the spinal degenerations commonly associated with primary optic atrophy. However, there can be but little doubt as to the cause in this, and that the loss of the knee-jerk was due to the same cause is probable. The absence of pigmentation of the skin is rather unusual.

Mercurial poisoning is not quite so common in its chronic form, but like lead and arsenic, perineural degenerations with evidences of peripheral nerve affections are in the majority.

Oppenheim compares the tremor of mercurial poisoning to that of disseminated sclerosis. Gowers describes the lateral tremor of the fingers as peculiar to lead. I have seen nystagmus in lead in the presence of other neurotic affections.

It should be stated with reference to the classic "blue" or "blue-black" line that it may or may not be present, according to the condition of the gums. It should be remembered that if it is present it is due to the fact that there is a separation of the gums from the teeth; that the line is due to the deposit of lead sulphide, and the sulphur is the result of decomposition of albuminous substances at this site. It may show, therefore, only over several teeth, over a great many or be entirely absent; but if distinct and at the margin, it should be considered as important evidence. It is probably not often blue, but more often black, and one gets the impression of blue, probably, from the red border of the gums; but whether blue or black is of minor importance, it is always a dark discoloration, and if at the margin of the gums, while it may not be conclusive, it should be regarded as strongly suspicious. Personally, I cannot recall another condition in which such a dark discoloration is present.

TREATMENT. In the treatment, iodides are used because of its effect in increasing the solubility in the blood, but a new danger arises, as was pointed out by Gowers, who cautions against the too free use of iodine, since the influence upon nerve structures is largely through the blood, and the throwing of a large quantity of the metal suddenly into the circulation may aggravate the symptoms.

Magnesium sulphate has long been known as a favorite eliminant. Calcium permanganate ($\frac{1}{4}$ gr. t. i. d.) is recorded to be of value by Stephens.¹⁹

A curious procedure recorded is the fixation abscess, which resulted in marked improvement, induced by V. Hinze²⁰ by subcutaneous injections of turpentine, 1 c.c. and 0.089 per cent. metallic lead recovered from abscess in 1.528 grams of pus.

¹⁹ British Med. Jour., May 14, 1910.

²⁰ Berlin. klin. Woch., June, 1910. No. 26.

The same precaution regarding the free use of iodides obtains in the treatment of chronic arsenical intoxication as with lead.

CONCLUSIONS. In closing, one may draw a few points from the observations, such as: 1. A wide variation exists in individual susceptibility to all metallic poisons.

2. In those susceptible, if the nervous system is attacked, the peripheral nervous system is the most vulnerable, and more especially the extensor supplies.

3. There is with lead poisoning, in all probability, an early lymphocytosis of the cerebrospinal fluid, and probably coincident with, or succeeding upon, the basophilic granulation of the red blood cells.

4. Non-inflammatory degenerations of any portion of the peripheral system should suggest the metals as a possible cause.

5. In the absence of skin evidences of arsenic and the blue line of lead, the urine, the blood, and finally artificial abscesses may be induced and examined for the metals; this procedure should, it would seem, lend itself as a diagnostic as well as a therapeutic aid.

6. A positive Wassermann reaction would not seem to exclude, especially lead, in favor of syphilis in primary nerve or tract degenerations.

7. The source of the poison may not be detectable until long after the presence of the metal as a cause, has been established.

I desire, in conclusion, to express my indebtedness to Dr. Melville Black for his valuable aid in studying the visual fields and the preparation of the perimetric charts which have been used.

THE METABOLISM, PREVENTION, AND SUCCESSFUL TREATMENT OF RHEUMATOID ARTHRITIS: SECOND CONTRIBUTION.¹

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In a previous communication² the writer advanced an hypothesis as to the general nature of rheumatoid arthritis, so called, and presented some metabolic and clinical observations upon three cases treated upon this basis. The tentative views there presented have been subjected to fuller consideration and development, and, in their application to a series of seventeen cases, form the substance of this paper. It may be well to repeat here some of the premises already stated:

¹ Reported before the American Association for the Advancement of Clinical Investigation, Washington, D. C., May 5, 1913.

² "The Metabolism and Successful Treatment of Chronic Joint Disease (Preliminary Report), AMER. JOUR. MED. SCI., October, 1912.

"It is a familiar clinical fact that chronic joint troubles form one of the most frequent and rebellious of diseases. The application of laboratory methods to the diagnosis of the several varieties and the rational treatment dependent upon it have reduced many of these to categories which are fairly well understood and yield good results. Thus the tuberculous, Neisserian, and specific joints tell their own story, but after eliminating them there remains a large class in which but little progress has been made. This is the class grouped by various writers under the headings, rheumatoid arthritis, chronic articular rheumatism, arthritis deformans, and so on, conditions having in common an obscure or doubtful etiology and a prognosis for the most part unfavorable.

"The activities of certain workers, particularly perhaps Goldthwaite and his collaborators in this field, have brought some order out of chaos, but it should be noted in passing, and with no credit to the internists and laboratory men, that it remained for orthopedists to suggest the simplest classifications and to practise the most rational therapy. It is due chiefly to the above men, for example, that we recognize in these obstinate cases the importance of a focus of infection in a tooth or tonsil, and that regulation of the diet along broad and intelligent lines is of value in the undernourished and overfed."

Lane, of London, has claimed that some of these cases are benefited by resection of the colon, but how or why this is beneficial is not clear. The matter will be referred to later.

"Grouping these cases as a whole, however, and eliminating them in turn from consideration, there remains a large and distressing number of cases which progresses from bad to worse despite all efforts.

"The principles of treatment as outlined above are now generally observed and practised by careful clinicians, but that they often fail is well known.

"The necessity of treating a number of sufferers from these conditions convinced the writer of the desirability of some definite observations by clinical and laboratory methods from which an etiology and treatment could be deduced.

"It is advised by many, for example, that in the dietary supervision incidental to good hygiene consideration should be had as to constipation, flatulence, the caloric need of the thin individual and the caloric surfeit of the fat individual, and that only the digestible foods should be eaten, that abundance of water should be ingested, and the like. At last analysis, however, these instructions are too generic, and in application fail of their purpose.

"The writer has observed in a number of instances the beneficial effect of purgation and starvation upon the subjective symptoms of certain joint cases, and the question is raised as to whether this be due to the absence of food decomposition and synthesis, to a diminution of intestinal bacterial activity, or to both. That the

amount of food *per se* is an important factor apart from its relation to bacterial activity is indicated somewhat by the well-known favorable action of arsenic in these states, one action of which is probably to hasten the general metabolic processes. Another agent capable of this same action, though to a greater degree, is thyroid extract, whose gradual effect on nitrogenous exchange and the persistence of this after administration of the drug has ceased, are testified to by many observers."³

On the basis of the reports of Lane and the not infrequent association of enteroptosis with joint disease, many have regarded the intestinal tract as related to this condition, but the manner of association has not been demonstrated.

Dietary control has been attempted in nearly every conceivable way, and has always failed, for the reasons to be later advanced. It is a conservative statement to say that, with the exceptions above noted, there has been to date no known successful therapy for arthritis deformans, and were any proof of this needed it could be found in the histories of most of the many sufferers from this disease, and, in particular, in the previous medical histories of cases here presented:

"It is plain, therefore, that a great reduction of the food intake, or the administration of agents which hasten the general body metabolism act beneficially on the symptoms of these conditions. The last mentioned agents, furthermore, are often beneficial even in conjunction with little or no reduction of the ingested food and may even stimulate the appetite to a greater consumption. If we apply the reasoning here suggested it would seem likely that there is a point at which one or all of the elements of food can be assimilated with satisfaction to the body needs and without detriment to any particular structure.

"Having found such a dietary regimen there would be offered thereby an opportunity for study of the processes active for good and evil which might yield facts of value. Why such a study has not been attempted before is not clear to the writer, since opportunity has at times presented in those cases which have yielded to the correction of intestinal ptoses.

"Reference to the literature, however, indicates that while the contributions to chronic joint diseases have been legion, they have rarely been along the lines indicated, and have rarely been accompanied by careful laboratory studies.

"The lesson to be learned is in some respects like that taught by gout and diabetes, though the particular elements harmful in joint disease must yet be determined. An effort was made along these lines, beginning with the simplest of foods in order that the effect of their several component elements might more clearly be observed."

³ Von Noorden, *Metabolism and Practice of Medicine*, iii, 991.

Milk suggested itself, of course, as the basis of experimentation, and was largely used in the first four cases treated. Owing, however, to the fact that the first case was that of a private patient, to whom buttermilk had been successfully administered, a complicating factor was introduced by adhering to it in the next three cases. The results were satisfactory clinically, but the issue was clouded by the introduction of the question of the intestinal flora. Suffice it at this point to say that subsequent experimentation and metabolic observations showed this to be an entirely unessential factor. The facts elicited by this study and their interpretation can probably best be approached by a recital of the series of cases.

Cases I, II, and III, with certain metabolic findings, have already been published (*loc. cit.*) and are not here included. Case I remains well (November, 1913). Cases II and III have disappeared from observation.

CASE IV.—Mrs. X., aged about thirty-eight years; mother of two healthy children. Referred by Dr. James E. Talley. This patient presented an unimportant previous history apart from the present illness, which began about four years before admission, and had progressively involved the hands, elbows, shoulders, knees, and feet. She had tried a variety of treatments, and had been told by her regular physician, who sent her to Dr. Talley, that he could do no more for her. There were soft tissue swelling and deformity of the hands, wrists, knees, and feet, and the patient complained of much disability and pain, especially at night. This awoke her frequently, and prevented her turning or assuming different postures. Her general physical examination was negative, as were also her blood, urine, and blood pressure, and on admission her weight was 140½ pounds. At no time had she fever. X-ray⁴ examination of her abdomen showed the head of the colon to be low in the pelvis, and the colon to be elongated, ptosed, and kinked. The stomach was also dilated and ptosed below the crest of the ilium. There was some demonstrable arthritis of both hands and slightly more of the elbows.

November 3, 1912, she was placed under the following regimen:
6 A.M.: 1 glass of buttermilk.

Breakfast: 2 apples; 2 pieces of toast and butter; 1 glass of buttermilk.

9.30 A.M.: Colonic lavage, with 2 quarts of normal salt solution.

10.30 A.M.: 1 glass of buttermilk.

Dinner: 1 orange; 1 bowl of tomato soup; 2 glasses of buttermilk; lettuce and tomatoes.

3.30 P.M.: 1 glass of buttermilk.

Supper: 1 piece of toast and butter; stewed fruit; 1 glass of buttermilk.

8.30 P.M.: 1 glass of buttermilk.

Aromatic fluidextract of cascara sagrada at bedtime.

⁴ Dr. W. S. Newcomet made all the x-ray plates and interpreted the findings.

November 5. The caloric value of her food approximated 1748 calories, which was about 12.5 calories per pound of body weight,⁵ or 27.5 calories per kilo body weight. She was given an option of spinach, celery, or tomatoes for the mid-day vegetable. The notes of her condition and dietary follow:

November 7. The stewed fruit was ordered given without sugar.

November 8. The improvement which had been suggestively present for two days was definite. She had no pain the previous night in her right shoulder nor in the neck for the first time in ten weeks. Did not feel stiff on waking. Hands were less sore and fingers could be moved more freely. Skin was somewhat wrinkled over the knuckles of the hand.

November 10. Apparently worse yesterday, as she had a poor night, but seemed better again. Fingers seemed more flexible than at any time yet. Complained of pain in the muscles along the shaft of the right arm and around the shoulder. Some "slip" and grating of right shoulder. Slight nausea complained of. Said her feet gave her no pain at all.

November 24. No pain for several days. Stiffness and soreness still on waking. Better than at any time since a gastric upset ten days ago. Walked entirely freely. Tongue was cleaner. Had a good night the last two nights.

November 29. Patient weighed $137\frac{1}{2}$ pounds; felt well enough to leave the hospital, and did so, but resumed rather strenuous domestic duties in the care of her children. Furthermore, she lived at a boarding house, and careful adherence to or observation of her diet was no longer possible, though she did the best she could.

December 1. Could button her children's shoes better than formerly, and her husband noticed that the swelling has gone from her hand.

December 3. Weight, $142\frac{3}{4}$ pounds, dressed.

December 7. Relatively, the left hand was worse.

December 12. Not so well or at least no better. Conditions of life were not as salutary as at the hospital.

December 23. Weight, $142\frac{3}{4}$ pounds. Walked fairly well and said she had had pretty good nights, with occasional exceptions. Fingers were rather stiff, but were not much swollen. At this point she disappeared from observation.

Comment upon this case will be made later.

CASE V.—W. S., aged seventeen years, rather slightly built, a student of illustration, was referred by Dr. F. H. Klaer. Admitted November 24, 1912. The patient had been treated at the dispensary of the hospital of the University of Pennsylvania for about three months without any substantial benefit. About four months previously, in July, he began to have stiffness and pain in a number of joints, which progressed from one to another until the right shoulder, both elbows, ankles, knees, and the fingers

⁵ Pounds have been used in weighing patients, as the hospital scales were so graduated.

of both hands were involved, making it difficult or impossible for him to use a pencil. The middle phalanges of all the fingers were swollen and broadened, but, in general, the bony change was not marked. He put his coat on slowly and with difficulty, because of the stiffness of the shoulders, and complained of considerable pain at night. In June, 1912, he had an attack of tonsillitis, which kept him two weeks in bed, but he apparently recovered entirely from it. Three weeks later, however, the result above noted occurred. At the University of Pennsylvania Hospital dispensary search was made for a possible focus of infection, and, in line with this, his tonsils were removed without benefit. The boy was intelligent and presented no obvious errors of hygiene. He was the holder of a number of championships with the rifle, and had always been active physically. The urine, blood, and blood pressure were normal. The x-ray examination of the abdomen showed the large bowel to be elongated and doubled on itself, with a kink in the splenic flexure. The caput coli was lower than normal. The hands showed a marked inflammatory arthritis, with slight atrophic and hypertrophic changes.

This case was deemed a suitable one in which to study the metabolism during illness and convalescence, as in Case III (*loc. cit.*). He was accordingly put on a "metabolic" diet of known value, and instructed to decide how much food he desired and then to adhere to it. After a few days of probation he settled down to the following: Breakfast, dinner, and supper were identical, and consisted each of bread, 64.5 grams; 1 egg;⁶ rice, 125 grams; butter, 9 grams; sugar, 10 grams; salt, $\frac{1}{2}$ gram; milk, 200 c.c.; water, 800 c.c. per diem. This dietary was continued for twelve days, and examinations were made with respect to the following: Nitrogen of the urine; ammonia of the urine; chlorides of the urine; ethereal, preformed, and total sulphates of the urine; depression of the freezing-point of the urine (Δ); titratable acidity of the urine and the nitrogen of the feces.

The figures for the respective days follow later, and will be discussed separately.

Upon completion of this period he was placed upon the following:

December 10. 6 A.M.: 1 glass of whole milk.

Breakfast: 1 piece of toast and butter; 1 apple or orange; 1 cup of chocolate (made with milk and sugar).

10 A.M.: 1 glass of milk.

Dinner: 1 bowl of strained vegetable soup; 2 glasses of milk; 1 serving of spinach.

4 P.M.: 1 glass of milk.

Supper: 1 piece of toast and butter; 1 glass of milk; 1 dish of unsweetened stewed peaches.

8 P.M.: 1 glass of milk.

⁶ The eggs varied between 42 and 53 grams, but the correct weights were, of course, utilized in working up the dietary totals.

He was given the option at lunch of any one of the following instead of spinach: Lettuce, with oil and vinegar; parsnips, beets, cabbage, cauliflower, turnips, stewed celery, served without cream gravy.

December 17. Second glass of milk at supper was stopped and replaced with one slice of stale toast and butter.

December 20. Onions or tomatoes at lunch; ice-cream twice a week; stopped glass of milk at 6 A.M.; to breakfast added 1 soft-boiled egg.

December 27. Stopped milk at 4 P.M.; added a small piece of white meat of chicken at supper.

January 3, 1913. Stopped milk at 10 A.M. and 8 P.M.

January 8. Alternated small lamb chop with chicken at supper.

January 15. Alternated steak and fish at supper.

January 16. Small roasted potato at lunch.

January 17. Oysters at supper when desired.

January 19. Small amount of oatmeal and cream at breakfast and small amount of sugar added.

January 23. Small amount of rice at supper, with butter added.

February 1. Complete diet: Breakfast: Small amount of oatmeal and small amount each of sugar and cream. 1 apple or orange; 1 egg (boiled, fried, poached, or scrambled); 1 glass of milk; 1 piece of toast.

Dinner: 1 bowl of vegetable soup; 1 small roasted potato; 1 glass of milk or junket; 2 pieces of toast and butter; 1 serving of any of the following vegetables: spinach, lettuce, stewed celery, cabbage, beets, turnips, cauliflower, parsnips, onions, tomatoes. No flour or cream gravies. Ice-cream twice a week.

Supper: 1 glass of milk; 1 piece of toast and butter; 1 dish of unsweetened fruit (apricots, apples, prunes, or peaches); 1 helping of any of the following: White meat of chicken (small amount), small chop, small piece of steak, fish (small amount), one dozen oysters (raw or panned), 1 helping of rice and butter and salt.

The ward notes indicated his progress as follows:

December 11, 1912. Fingers were a little better, especially in the left hand. When asked to compare his condition with what it was when he first came to the hospital, he said, after a moment's thought, "I would say I am very much improved." Could walk around the yard. "Even the patients who sit on the porch remarked the improvement in walking." Helped the nurses do little things in the ward. Had had no medicine since admission except cascara for the last three days at bedtime.

December 19. Slight headache. Could bend his finger better and touched the thenar eminence for the first time with it.

December 27. Went home Christmas, and was pretty active, walking considerably for seven hours. Had some pain in his heels at bedtime. Went up stairs two steps at a time easily, but had

great pain in tendo Achillis on descending. He was kept in the hospital only to accustom him to exercise and greater range of food.

January 7, 1913. Hands were better than they had been since admission; he could open and flex them with great rapidity and ease. Day was warm, damp, and rainy, but he seemed to have

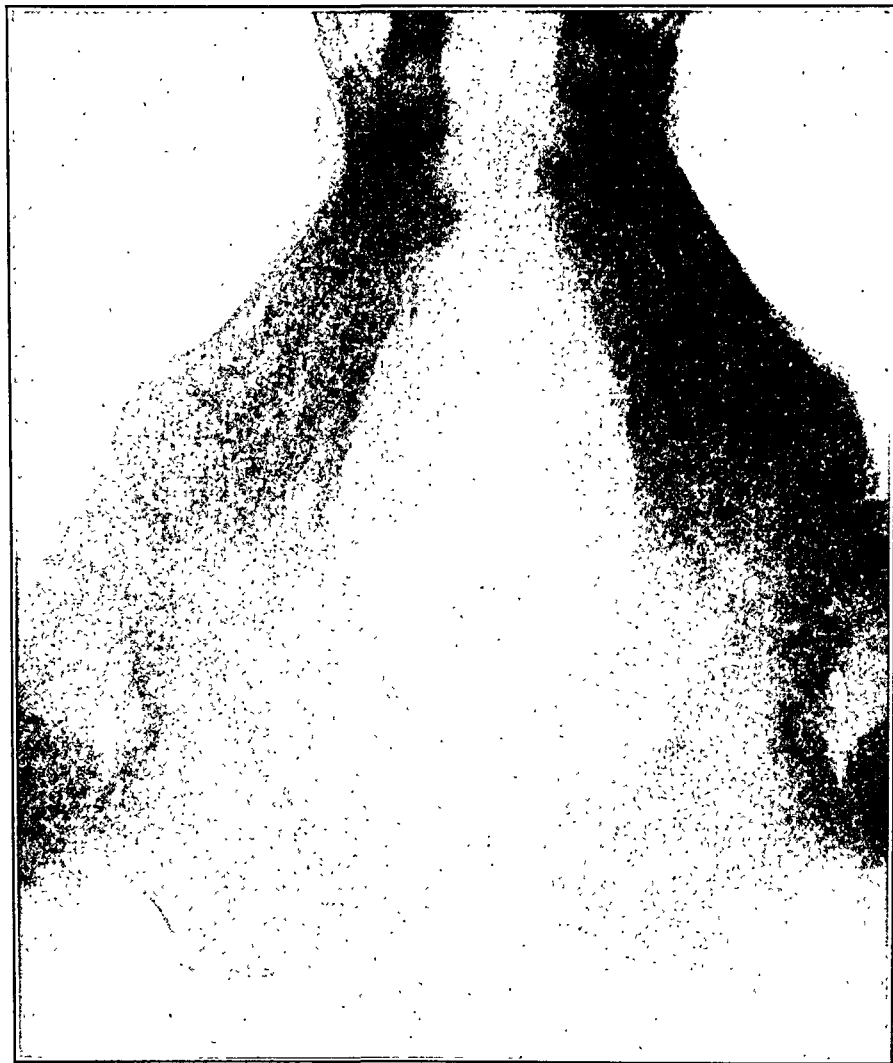


FIG. 1.—Feet of Case V. Notice erosion of left heel.

no particularly deleterious effects from it, as was usual when his joints were not so well.

January 27. Raw and rainy. Felt slight ache in muscles. Joints were all well. Went home the previous day and walked twenty-four squares. Milked three cows and was pleased at the full use of his hands. Weight $123\frac{1}{2}$ pounds, which was more than for four months past and $6\frac{1}{2}$ pounds more than on admission.

January 29. Hands, shoulders, limbs, etc., felt well. Had pain in both heels, especially the right, where there appeared to

be an exostosis posteriorly. The x-rays later showed this to be an osteoporosis, with a distinct hole in the bone.

February 11. Went skating in the park for one hour, also three days previously for one and three-fourths hours. Skated pretty hard. Heels steadily improving.

February 15. Discharged.

February 28. The patient returned for observation, and was in excellent shape.

He was sent for on June 11, 1913, and said that he was as well as before he was affected with arthritis. Sometimes at night after working all day he felt a slight soreness in the heel, but this was decreasing and was felt only occasionally. Two days before, on June 9, he had piled up in the field about two and one-half tons of bales of rye, which indicates freedom of movement in joints and muscles. His weight was $124\frac{1}{4}$ pounds, 4 pounds less than when in the ward. This loss was probably owing largely to his hard work, but also to a fall from a horse, in which he injured his wrist. He was nauseated and shocked, and for some days was "off his feed," following the accident. It will be noted that colonic lavage and buttermilk were omitted entirely in this case. This point will be discussed later. On October 4, when seen, he was actively engaged in teaching, and was very happy in his present condition of health.

CASE VI.—Mrs. H. L., aged about fifty-eight years. Admitted to the hospital on December 31, 1912. Referred by Dr. Francis O. Allen. The patient had excellent health until the onset of the present trouble, four years previously. It began in the ankles and progressed to the arms, hips, hands, and wrists, the latter two becoming involved chiefly during the past year. Physical examination revealed myocarditis, a slight systolic apical murmur, and some cardiac hypertrophy, with a blood pressure of 202 systolic and 110 diastolic. There was distinct though no great swelling on the dorsum of each hand and wrist and over some of the knuckles.

She complained of tenderness on pressure at these sites, and of pain upon motion of arms or legs, making all activities a burden and an effort. Appetite, sleep, and bowels were undisturbed. Her weight was $151\frac{3}{4}$ pounds. Her blood and urine were essentially normal, and the latter was at all times free from indican. She had no fever. The x-ray examination revealed both stomach and large bowel to be greatly elongated and ptosed. The bowel was tortuous, especially at the splenic flexure where it crossed the stomach and divided the latter in half. The joints and bones of both hands and wrists showed both atrophic and hypertrophic changes, with some inflammatory involvement.

Treatment was instituted on January 4, 1913, with daily colonic lavage and the following dietary:

Breakfast: 1 apple, 1 egg, 1 piece of toast, and 1 piece of butter.

Dinner: 1 bowl of broth, stewed tomatoes, and an apple baked

without sugar. In place of tomatoes she was given an option of spinach, celery, parsnips, or turnips.

Supper: 1 egg, 1 slice of toast and butter, 1 helping of stewed fruit (made without sugar), and 1 glass of milk.

This yielded about 1000 calories or about 7 calories per pound of body weight or 15 calories per kilo. This diet was changed as follows on the days indicated:

January 10. Lettuce, with small amount of French dressing, at supper; celery stalks once daily.

January 14. 1 glass of milk at breakfast.

January 21. Stopped glass of milk at supper and substituted one small roasted potato.

January 22. Gave small piece of chicken at supper.

January 23. Celery at lunch instead of supper. Alternated with chicken, a small chop, or small amount of beefsteak or fish.

January 27. Stopped 1 glass of milk at breakfast and gave 1 slice of toast additional.

February 3. Gave a total of two green vegetables at lunch.

February 12. Gave stewed fruits made with sugar.

February 16. Small dish of oatmeal and cream at breakfast, and stopped 1 slice of toast.

February 17. Gave colonic irrigations every other day instead of daily.

February 19. Small amount ice-cream thrice weekly instead of stewed fruit at lunch.

February 27. 1 apple at bedtime; 6 panned oysters at lunch daily.

February 28. Beans or peas instead of potato at supper optionally.

March 7. Meals averaged as follows:

Breakfast: 1 medium-sized apple; 2 tablespoonfuls of oatmeal; 1½ ounces of cream; 1 poached egg; 1 piece of toast; 1 piece of butter (6½ grams); 1 cup of coffee (f5ij coffee, f5ij cream, 1 cup of hot water; she preferred no sugar).⁷

Lunch or Dinner: f5ix of clear soup; 6 panned oysters; 2 tablespoonfuls of spinach; 2 tablespoonfuls of stewed tomatoes; 2 stalks of celery; 6 stewed figs and 1 tablespoonful of juice.

Supper: 2 pieces of toast; 1 piece of butter, 6½ gram; 2 tablespoonfuls of beans; 2 broiled lamb chops (small); 1 dish of lettuce and 1 tablespoonful of mayonnaise dressing; 2 tablespoonfuls of apple sauce.

Her progress, as indicated by almost daily notes made at the time, follows:

Diet begun January 4, P.M.

January 5. No change, except that hand was slightly more sore, possibly because of the rather raw day.

⁷ The liquid measurements are often given in drams and ounces as this was more convenient for the nurses. The food weights are always in grams.

January 6. No definite change. Possibly less pain in metatarso-phalangeal joint of left little finger and also possibly slightly less swelling. She had pain the previous night.

January 7. Pain in the left hand was less on pressure. The right hand was about as the day before. The shoulders hurt less during the night, and were better this date.

January 9. Patient said she felt "very spry." Hands were distinctly less tender to touch and seemed reduced in size. The skin over them was more wrinkled, and she had had but little pain in shoulders and none elsewhere. Knees did not hurt at all.

January 16. Patient said she was surprised to notice rain in the night, as her joints had failed to forewarn her of it for practically the first time in six months. Hands improving and she felt well. No ache in the arms.

January 25. Slightly more pain on pressure over the wrist sore points. Was slightly "conscious of her bones" during the night.

February 5. Walked nine squares in the morning. Wrists were better than they had been to date. Slight stiffness in the middle finger of left hand and little finger of the right hand.

February 23. Patient noticed that she had caught a "cold," with sore throat, malaise, fever, aching in bones with headache and stiff neck the two previous days. Felt better. Bowels had been well moved. Joints *per se* were no worse than the rest of her bones (which ached) during the attack. In bed two days.

February 25. Up and out. Felt a little "weak," but joints were all right. Given quinine, gr. ij, t. i. d.

March 4. Received more than she wanted to eat. Pain difficult to find on pressure, and the patient was really entirely well. Had been kept in the hospital only to instruct her "how to live." Quinine was discontinued.

March 8. Discharged from hospital. Weight, 150½ pounds.

The subsequent course of this patient was that upon getting home she took liberties with her diet within the first twenty-four hours, having had among other things a "charlotte russe." She appeared at once for treatment because of slight sensitiveness in the arms. After leaving the hospital she lived under unfavorable conditions, occasionally skipping a meal or substituting things other than those ordered. It was found nearly impossible in this case to insure the patient's getting the exact dietary prescribed, though she adhered to it in the main, and kept in fair shape, leaving for the South on May 12, weighing 142¾ pounds. At this time the only evidences of her trouble were some tenderness on pressure over the sore spots on the wrists and a slight premonition in the shafts of her arms of a "change of weather." She felt active and in excellent health, and was urged to be more careful in her diet. Advice by letter from her home in the South on August 7 reported her entirely free from pain anywhere and feeling perfectly well.

(To be continued.)

REVIEWS

MEDICAL MEN AND THE LAW. A MODERN TREATISE ON THE LEGAL RIGHTS, DUTIES, AND LIABILITIES OF PHYSICIANS AND SURGEONS. By HUGH EMMETT CULBERTSON, ESQ., member of the Ohio and New York Bars; Contributing Editor to many legal publications. Pp. 325. Philadelphia and New York: Lea & Febiger, 1913.

THIS work represents an effort on the part of the author as set forth in the preface to present the main features in modern law as it pertains to physicians and surgeons. The need for such a work is manifested in the utter lack of knowledge of the law as it bears upon medical matters shown by the average practitioner and his consequent inability to properly discharge many of the duties arising from his position as an advisor either to his patients or the community.

The author has combined the main points wherein medicine and law touch each other, based on actual court decisions. The discussions deal with every possible phase of medical law and are expressed in an unusually clear, concise, and interesting manner. Each chapter represents more or less a dissertation on one particular phase of this subject. The questions of qualifications for practice, compensation, malpractice, criminal liability, physicians and surgeons as witnesses, and wills are the titles of some of the especially interesting chapters. The table of contents and index make reference to any subject simple and easy. As a reference book for physicians or as a compend for lawyers the book should have a high place. The book is well printed on heavy paper and contains very few typographical errors.

F. H. K.

OBSTETRICS. By W. P. MANTON, M.D., formerly Professor of Obstetrics and Clinical Gynecology, Detroit College of Medicine; Gynecologist to the Harper Hospital. Second Edition; Pp. 292; 97 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THAT this little book has attained its purpose is evidenced by the appearance of a second edition. While such a manual is in-

tended primarily for the student, the author has so carefully revised the book that it should prove helpful to the practitioner as well. Although limitations of space have forced the curtailment of some subjects, yet the important fundamentals have been well presented. Appended to each chapter is found a list of pertinent questions as an aid to the student in rapid review work. The principles stated governing the management of pregnancy, the conduct of labor, and the choice and technique of operative procedures are in accord with the best modern ideas. The recommendation of atropine in doses of $\frac{1}{10}$ grain in the treatment of salivation as mentioned on page 69 is no doubt due to a typographical error. The illustrations are well chosen. The book should continue to find favor among those who wish a small, accurate manual of obstetrics suitable for quick reference work.

P. F. W.

THE PRINCIPLES AND PRACTICE OF GYNECOLOGY. FOR STUDENTS AND PRACTITIONERS. By E. C. DUDLEY, A.M., M.D., Professor of Gynecology, Northwestern University Medical School; Gynecologist to St. Luke's Hospital, Chicago. Sixth edition. Pp. 795; 439 illustrations and 24 full-page plates in colors and monochrome. Philadelphia and New York: Lea & Febinger, 1913.

RECOGNIZED as an authority on the subject since its initial appearance fifteen years ago, Dudley's Gynecology presents in the sixth edition a thoroughly modern text-book embodying all the recent advances in gynecology. In this edition the text has been subjected to a careful revision, thus allowing the introduction of much new material without increasing the size of the volume. The book possesses a wealth of original and accurately executed illustrations, certain series of which serve to portray step by step the various stages of different operative procedures, twenty-five drawings and diagrams being used to explain the operation of perineorrhaphy.

The classification of the subject matter follows that of previous editions. Thus instead of all the pathological conditions of an organ being included under such a heading we find the infections and inflammations of the pelvic organs following one another in the manner of their etiological and pathological sequence. The first part of the book devoted to the general principles concludes with a chapter on the relation of dress to the diseases of women, discussing briefly the perversion of pelvic physiology by the present-day manner of dress and living. The author defines clearly the uses and the limitations of local therapy and cautions especially against the improper and often unsuitable use of intra-uterine medication. His personal experience is expressed in the preference for the expectant and palliative, rather than the surgical treatment, curettage, in acute metritis,

Mention is always made of x -ray therapy in those conditions amenable to its influence, but it may not yet be accepted as a substitute for operative measures in myoma. The use of the x -rays and of radium is to be restricted to the palliative treatment of inoperable or carefully selected cases of myoma and other tumor formations. Beside the operations personally preferred by the author in the treatment of displacements of the uterus, other well known methods are fully described and illustrated. Worthy of note is the inclusion of the highly favorable results obtained in another clinic with the operation devised by the author for the relief of pathological antelexion of the uterus, and its accompanying dysmenorrhea and sterility. In the chapter on diagnosis and treatment of bladder lesions some cystoscopes more recent than those described might have been mentioned. The final section on disorders of menstruation and sterility closes with a chapter discussing an original plastic operation for the treatment of incontinence of urine.

The book is a splendid exposition of gynecologic, especially plastic, surgery, and this edition fully maintains the eminence established by its predecessors.

P. F. W.

"THE BRAIN AND SPINAL CORD." A MANUAL FOR THE STUDY OF THE MORPHOLOGY AND FIBRE TRACTS OF THE CENTRAL NERVOUS SYSTEM. By DR. EMIL VILLIGER. Translated by GEORGE A. PIERSOL, M.D., Sc.D. Philadelphia and London: J. B. Lippincott Co.

THERE are many excellent works on the brain and spinal cord in the German and French languages, but really adequate expositions of the subject in the English language are rare.

The selection of Villiger's work for translation was wise and timely. In the original it lacked the encyclopedic character found in other well-known anatomies, thereby gaining as a text-book.

The work is divided into three parts: Part I.—Morphology; Part II.—Fibre-tracts; Part III.—Serial Sections of the Brain Stem.

Ninety-three pages are devoted to the first part in which the student is never allowed to lose sight of the embryology of the cerebrospinal axis. The illustrations are numerous and for the most part excellent. The section dealing with the cerebellum (pp. 72 to 77) is illustrated with figures possibly more diagrammatic than accurate. For instance, the relation of the pyramid to the lobus biventer is hardly borne out in the human brain. In the text (p. 75) one finds the following regarding the secondary flocculus: "Lateral to the latter, between the lobulus quadrangularis of the

superior lobes and the lobulus biventer is seen the accessory flocculus, flocculus secundaris." That the parafloccular mass is sometimes found in the human subject in a very rudimentary condition is possibly true, but careful search will often fail to discover what is so well marked in some of the lower animals.

In the second part the first six pages are devoted to the methods of studying the fibre-tracts. This also is wisely flavored with the embryological point of view. The illustrations of Part II are beautifully clear and the text critical and excellent. For instance, the subject of taste-conduction is dealt with in the following manner: the several theories are lucidly stated, the last to be given (chorda, geniculatè, intermedius, medulla) being introduced by "Finally, according to the view which seems, perhaps, the most reasonable," etc. This careful conservatism is the key-note of the book.

The third and last section presenting sections of the brain stem from the anterior end of the corpus callosum to the quadrigeminal region; from the caudal end of the medulla oblongata to the quadrigeminal region and one sagittal plane leaves nothing to be desired in accuracy and definition.

The whole work is a credit to the author, translator, and publisher, and can not fail to excite the enthusiasm of the student.

A. R. A.

A CLINICAL MANUAL OF MENTAL DISEASES. By FRANCIS X. DERCUM, M.D., Ph.D., Professor of Nervous and Mental Diseases, Jefferson Medical College, Philadelphia. Pp. 425. Philadelphia and London: W. B. Saunders Co., 1913.

THERE is no one who is better qualified to write a practical book on insanity than Dr. Dercum, for he has had a large experience with insane patients and has taught medicine for years. There is indeed a need for a short practical book such as this, for the student has little time to read a larger work, and the average practitioner even less. To them it is a question, is this man insane or not, and how can I recognize that he is insane? At the present time there is a widespread tendency to abandon the older classifications and conceptions of insanity. This is due largely to the work of Freud, Bleuler, Jung and their followers. Whether one believes in their teaching or not, and Dr. Dercum does not, it would be folly to attempt to teach their theories to the average medical student.

The subject matter is well arranged and presented in a logical and comprehensive manner. It is eminently a book for students and medical practitioners, and can be highly recommended.

T. H. W.

GLYCOSURIA AND DIABETES. By FREDERICK M. ALLEN, A.B.
M.D. Boston: W. M. Leonard, 1913.

THIS remarkable book of nearly 1200 pages, combines an excellent presentation of the literature of diabetes and the results of experimental work on 200 dogs, 200 cats, and a smaller number of rabbits and guinea-pigs. The style of the writing is clear and, for the most part, absolutely convincing. If the experimental work is confirmed, the book will rank as a classic on the subject. No one interested in diabetes as a scientific problem can afford to be without this volume.

Allen's investigations were along two lines: (1) The behavior of sugars in the body, and (2) the production and modification of diabetes.

The various methods to determine sugar tolerance were first tested and preference was given to that of subcutaneous injection. In the normal animal the subcutaneous tolerance of levulose was a small fraction of that of dextrose. It was found that neither diabetes nor its complications could be produced in normal or predisposed animals by prolonged excess of dextrose. The "paradoxical law" is thus enunciated; the more sugar given, the more utilized. All types of non-diabetic animals follow this law and it holds true with alimentary, hunger, toxic, phlorhizin, adrenalin, thyroid, and nervous glycosurias. Hence, these are not diabetic conditions, for there is a true limit of tolerance in the diabetic organism. Furthermore, if the common sugars are given orally to normal animals, they have an antidiuretic effect and the same effect is produced when sugar is given in the above named glycosurias. The administered sugar acts as if it were in colloid combination in the blood. But if sugar be given to the truly diabetic, diuresis at once sets in, the sugar behaving like a crystalloid. This test proves that diabetes cannot be due to an overproduction of sugar.

As regards the second experimental portion of the book, the author distinguishes between diabetes gravis, which follows uncomplicated removal of nine-tenths of the pancreas and in which dextrose is excreted on a meat diet, and diabetes levis, in which a seventh or an eighth of the pancreas remains in position and dextrose is excreted on a starchy but not on a meat diet. When a sixth of the pancreas is left, a transient diabetes may ensue but never a permanent one. After establishing these facts experimentally, dogs were prepared which were not diabetic nor yet could develop diabetes in the ordinary course of events, but which had so little surplus of pancreatic tissue that untoward influences might render them diabetic. In this condition the following influences proved to be negative factors so far as inducing diabetes was concerned; alimentary glycosuria, acid intoxication, toxic glycosurias,

phlorhizin glycosuria, excess of epinephrin or thyroid administration as well as operative reduction of adrenal or thyroid tissue or both, and certain nervous and circulatory alterations. These experiments strike a hard blow at the polyglandular doctrine of von Noorden and his pupils, and show it to be out of harmony with the facts. The only influences found which induced permanent diabetes in the predisposed dogs were: (1) Bernard's puncture which was followed by the characteristic changes in the islands of Langerhans; and (2) a disturbance in the blood supply to the pancreas which occurred after rapid obliteration of the portal vein. It was found that ligation of the pancreatic ducts in dogs with pancreas remnants, tended to the preservation of the islands of Langerhans and the advisability of the enervation of the pancreas remnant is also suggested in order to remove the nervous effects. In the author's mind the sequence of causation of human diabetes is to be expressed as follows: Nervous disorder, impaired function of the islands of Langerhans, deficiency of the pancreatic amboceptor, glycosuria, and other symptoms.

This book, the work of a hitherto unknown author, is a credit to American medical science and to the Harvard Medical School, in which it was accomplished.

G. L.

DISEASES OF THE STOMACH, INTESTINES, AND PANCREAS. By ROBERT COLEMAN KEMP, M.D., Professor of Gastro-intestinal Diseases in the New York School of Clinical Medicine. Second Edition. Pp. 1021; 388 illustrations. Philadelphia and London: W. B. Saunders Company, 1912.

THE first edition of this text-book was favorably reviewed in this JOURNAL in 1911 (N. S., cxlii, 892). It was suggested at that time (not by the present reviewer, however) that the book might well include a consideration of diseases of the liver and pancreas. In the new edition the author has followed this suggestion so far as the latter organ is concerned and has devoted a little over 100 pages to the subject. He has also devoted a chapter to infections by the *Bacillus coli* and has rewritten the article on duodenal ulcer in accordance with the views of recent authorities on the subject. The chapter on Methods of Diagnosis in pancreatic disease contains a rather full account of the numerous tests that have been suggested. Fortunately for the general practitioner the author emphasizes a very few methods which he considers of value: the examination of the motor and secretory functions of the stomach, the general test of the intestinal functions by the Schmidt-Strassburger diet, the Boldyreff (or Volhard) method of securing the pancreatic juice, the examination of the urine for sugar, the fecal

findings after the administration of pancreatic extract and the examination of the blood for the rapidity of clotting. This volume covers its wide field with fidelity and for the most part sound judgment. It should be of use for reference particularly for those who do not have access to original articles and monographs. As stated in the previous review the references are more scanty than one would wish but this is a fault common to most American (and English) medical books and is probably to be laid at the door of the publishers and purchasing public rather than to the particular author concerned.

C. B. F.

A TEXT-BOOK ON THE PATHOGENIC BACTERIA AND PROTOZOA. FOR STUDENTS AND PHYSICIANS. By JOSEPH McFARLAND, M.D., Professor of Pathology and Bacteriology in the Medico-Chirurgical College of Philadelphia, etc. Seventh Edition. Pp. 878; 293 illustrations. Philadelphia and London: W. B. Saunders & Co., 1912.

DR. McFARLAND'S previous editions of this book were confined to bacteria but the growth of microbiology and the demands of friends of the book as well as of teaching, required an enlargement to include the pathogenic protozoa. The author lays out for himself in the preface the tasks of describing all the animal and vegetable microorganisms of pathogenic importance, with their mode of action, the tests necessary to show their presence, and the important techniques now in use. The treatment of the last is particularly succinct. In the various chapters upon the individual microbes, definition, habitat, morphology, and cultural characters are sufficiently covered but most attention is given to toxicity, pathogenesis, lesions, immunity, and treatment depending upon the last. Many references are given and all authors are treated with full consideration. The bibliographical list before the index is serviceable. The illustrations are excellent and each one means something. Dr. McFarland's style is, as usual, exact and pointed but fluently readable withal. The diseases due to the filterable viruses are nowadays considered with the infectious ones. A chapter on this subject is missing but the omission is not inconsistent with the task the author has assumed and fulfilled. It is to be hoped that it will be convenient to include this subject in future editions. The book in its present form is a welcome one and will be popular.

H. F.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Etiology of Relapse in Malarial Infections.—JAMES (*Jour. Infect. Dis.*, 1913, xii, 277) believes the asexual cycle alone is the cause of relapse in malaria. That the asexual cycle often persists in so-called spontaneous cures can be proved in numbers by finding the parasites by the thick film method. Infections insufficiently treated with small doses of quinine will relapse because the parasites of the asexual cycle in the spleen and bone marrow are little if at all affected. Early vigorous treatment is indicated, as the older the asexual cycle the more resistant to quinine it becomes. If parasites persist in the blood during treatment, faulty absorption of the drug is sure to exist, and the method of administration should be changed. It is easier to eradicate the infection in patients in good health because of the aid of the natural protective forces of the body. The practical importance lies in the guide to treatment. Among Americans in the Canal Zone, when liquid sulphate of quinine was given in doses of 20 grains a day by mouth, recurrent cases followed in large numbers at short intervals. For several years it was increased to 20 grains on diagnosis, and 10 grains three times a day for at least ten days. The number of recurrent cases was noticeably diminished, among the Americans but not sufficiently among the poorly nourished Europeans. A treatment was then instituted of 45 grains a day. This has practically eradicated malaria among the Americans, and to a large extent among the European laborers. The latter, however, treat mild infections themselves with small doses and so produce a relatively quinine-immune asexual cycle that is more difficult to eradicate. To stamp out the disease this vigorous, early treatment to prevent relapses is one of the most powerful weapons.

An Outbreak of Septic Sore Throat.—MANN (*Jour. Infect. Dis.*, 1913, xii, 481), in studying most completely an epidemic of septic sore throat in Concord, N. H., has convicted the milk supply again, as was the case in the Chicago, Baltimore, and Boston outbreaks. A streptococcus was the cause and tonsillitis with marked cervical adenitis the principal features. More adults were affected, however, than children. Mann emphasizes cream also as a great source of danger. It was clear that the milk was infected through handling by individuals suffering with the disease, and the cream when separated retained the infected organisms. He believes the standard of intelligence among dairymen is too low. The public should demand that the producers be able to recognize the importance of safe-guarding milk against bacterial contamination. It is just as important to safe-guard the cream supply. Under present standards it is not safe to use market milk in the raw state.

Meiostagmin and Epiphamin Reactions in the Diagnosis of Carcinoma.—BURMEISTER (*Jour. Infect. Dis.*, 1913, xii, 458) has applied Ascoli's meiostagmin reaction to the diagnosis of carcinoma. Considering the successful application by Ascoli and coworkers, and the few reports in this country, Burmeister's conclusions are especially interesting. He finds that a decidedly negative meiostagmin reaction is of more value than a positive one, and may be considered of some weight in ruling out carcinoma. A moderately or even strongly positive reaction is not necessarily indicative of malignant tumor. The epiphamin reaction is valueless in the diagnosis of malignant tumors. The results obtained by other workers who have employed the method in the diagnosis of conditions other than carcinoma are explained by the range of error. In no single instance were two like curves obtained by the same method for the same serum and antigen mixtures, even with distilled waters instead of antigen and antiserum the extremes of the range of error were too great for practical purposes.

Droplet Infection in Diphtheria.—FLÜGGE and his pupils have emphasized the importance of droplet infection in the spread of tubercle bacilli, but there has been no experimental work with reference to the emission of diphtheria bacilli. TEAGUE (*Jour. Infect. Dis.*, 1913, xii, 398) has obtained very interesting results in this regard. He exposed blood-serum-glucose plates about three inches from the mouths of diphtheria patients during coughing, singing, counting, and talking. Of 51 cases, 65 per cent. emitted viable diphtheria bacilli. The plates indicated that droplets containing viable diphtheria bacilli are emitted frequently by diphtheria patients in talking and coughing, but usually in small numbers. To prove that laryngeal cases emit vastly more droplets containing bacilli than pharyngeal and tonsillar cases, Teague's larynx, pharynx, and mouth were swabbed with *B. prodigiosus* at different times, and plates exposed during coughing. But results showed no more droplets thrown out from the larynx than from the mouth. *B. prodigiosus* in droplets have been borne in the air 53 meters along a corridor and up two flights of stairs, and even 600 meters on the breeze. Since *B. diphtheriæ* is much more resistant to drying, Teague assumes it would be carried even greater distances.

SURGERY

 UNDER THE CHARGE OF

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Anesthesia of the Brachial Plexus.—KULENKAMPFF (*Zentralbl. f. Chir.*, 1913, xl, 849) wishes to explain the disturbances which have been reported in connection with his method of anesthetizing the brachial plexus by injection with local anesthetic solutions. He has employed the method in over 200 cases, but has not met with the accidents reported. He admits that the patients complain, occasionally, of distress in the chest but not in the arm. In the introduction of the needle, as soon as it is turned backward and medialward, it is close to the plexus and usually produces paresthesia. He believes that this is due to an irritation of the first intercostal nerve which is chiefly concerned in the formation of the ulnar nerve. The needle may cause disturbance by perforation of the pleura, an accident which has been reported several times. Kulenkampff reviews the literature briefly in regard to the character of the disturbances reported and the various interpretations for them. He concludes that in all cases the disturbances were similar and accounts for them by an irritation of the pleura or of the first intercostal nerve. He has long been familiar with the same clinical picture, not in connection with anesthetization of the brachial plexus, but with the performance of paravertebral injection anesthesia. He has seen it in connection with thoracotomy, kidney operations, and transpleural drainage of subphrenic abscess. There is a brief and characteristic free interval between the first pricking sensation from the penetration of the nerve by the needle point and the later severe pain, which finally disappears. The second severe pain is regarded as reflex. Similar reflex effects have been observed in connection with the peritoneum, but more particularly with the pleura. Death has occurred from puncture of the pleura. With regard to the cases reported in which paralysis of the phrenic was supposed to have resulted from injection of the brachial plexus, Kulenkampff says that the evidence is lacking to show that the phrenic is particularly sensitive and possesses sensory fibers. He regards it as significant that the diaphragm has been divided painlessly without anesthetization of the phrenic nerve, if the intercostal nerves have first been anesthetized. This he has demonstrated himself in dividing the diaphragm in transpleural drainage of a subphrenic abscess. He believes that the disturbances reported were not due to a paralysis as maintained by several writers, but to either a pleural wound or a pricking of the first intercostal nerve.

A Study of the Pathological Anatomy and Physiology of Amyloid Degeneration of the Kidneys in the Tuberculous.—LEON-KINBERG (*Journ. D'Urolog.*, 1913, iii, 561) says that in the course of a chronic pulmonary tuberculosis, amyloid degeneration attacks the liver, spleen, and suprarenal capsules before attacking the kidneys. It is not rare to encounter in others massive amyloid disease, while in the kidneys only loops of the glomeruli or arteries of the pyramids are infiltrated with amyloid substance. At this period, except in cases with a preëxisting chronic renal lesion, there are in general no clinical symptoms of nephritis. Only albuminuria or at times an abnormal polyuria can attract attention to it. A study of the urinary secretion in these cases permits one to recognize an important syndrome. The percentage of urea is always very low, that of the chlorides below the normal. Yet the secretion of the chlorides and even that of the urea is sufficient. These signs are an evidence of an exaggeration of the power of concentration of the kidney, a kind of hypersecretion. When the histological examinations can be made under good conditions, there is found a particular hypertrophy of the cells of the cortical tubes, which seem to be the histological translation of hypersecretion. From the practical point of view it is believed that the establishment in a tuberculous patient of the urological syndrome described will often permit the diagnosis of amyloid degeneration to be made early, before the appearance of great edema, massive albuminuria, and uncorrectable diarrhea.

Thirteen Cases of Traumatic Rupture of the Spleen without External Wound.—NORLEIN (*Archiv. geb. d. Chir.*, 1913, vii, 520) from his study of the 13 cases which he reports and of the literature, says that the number of ruptures of the spleen that are brought to the hospital early enough to have some chance from a surgical operation, appear to increase rapidly. All surgeons should, therefore, be well informed concerning the etiology of the lesions associated, their symptoms, and their treatment. Although we lack pathognomonic signs of rupture of the spleen, it is nevertheless possible to make a probable diagnosis in the majority of cases. The best treatment is to make a median exploratory laparotomy incision, from which a transverse incision to the left is carried across the rectus, to expose and treat the rupture. Whenever possible, one should respect the integrity of the spleen. What is needed now in splenic surgery is the perfection of conservative methods and especially methods of suture.

An Instance of a Large Ureteral Calculus and Some Other Cases of Calculi.—WHERRY (*Brit. Med. Journ.*, May 17, 1913, 1043) reports an interesting case in which two large ureteral calculi were removed through the peritoneal cavity, with success. The patient was a girl, aged sixteen years, in whose condition there was little to call attention to her real malady. She had on admission, joint and epigastric pains swelling of the knee-joints on both sides and pain in the right side of the chest. The urine was acid, free of albumin and sugar. She was watched during five weeks until an access of fever and abdominal pain led to further examination of her urine, in which some pus and blood were found, and some crystals of oxalic acid. Digital examin-

ation of the rectum disclosed a large mass to the right of the uterus and the x-rays made it almost certain that there were calculi in the ureter. Through a median incision the abdomen was opened, and then with the patient in the Trendelenburg position two large calculi were found in the pelvic portion of the ureter. The stones were fixed and could not be pushed upward or downward. The ureter was clamped above, an incision was made, and the stones removed; about two ounces of purulent urine were swabbed out. The ureter was sewn up with catgut, using a harelip needle. The patient was then placed in the horizontal position and the suturing tested, so that the pressure in the ureters was tested in two positions. The clamp was removed and the abdomen closed in the usual way without the use of drainage. A good recovery was made, the temperature came down at once, and except for washing out the bladder with boric solution there was no trouble with the nursing. Together the stones measured $2\frac{1}{8}$ inches by 1 inch in diameter, and their weight when dry was 226 grains and 91 grains, or a total of 317 grains.

THERAPEUTICS

UNDER THE CHARGE OF

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Digitalis and Strophanthin Therapy.—SCHENK (*Wein. klin. Rundschau.*, 1913, xxvii, 375) recommends digistrophan which is a combination of digitalis and strophanthin for the treatment of disturbances of compensation in heart disease. Digistrophan has the advantage of combining the tonic action of digitalis with the regulating action of strophanthin in cases of failure of the cardiac muscle. Schenk claims that digistrophan is prompt in its action, certain in its effects, and stabile in its composition. He says that the remedy is easy to take, has no untoward effects, and deserves a wide use.

Three cases of Amebic Dysentery Treated with Salvarsan.—MADHAUS and HILL (*Jour. Amer. Med. Assoc.*, 1913, lxi, 385) report three cases of amebic dysentery in detail that were apparently cured by salvarsan. One of these patients had a positive Wassermann reaction and after receiving neosalvarsan together with mixed treatment the bowel movements became normal with no blood or mucus present, and no amebæ. In this patient there was no evidence of syphilis except possibly the fact that before the treatment the man was bald and since has developed an excellent growth of hair. The two remaining cases had negative Wassermann reactions and no clinical evidence of syphilis. They had contracted in the Philippines amebic dysentery which recurred frequently until it became practically a chronic con-

dition with acute exacerbations. Following the salvarsan treatment, a marked and prompt improvement occurred and in a comparatively short time the amebæ together with the mucus and blood disappeared from the stools. Madhaus and Hill say that it is perfectly evident that these three cases prove nothing, but the results have been so striking that it has seemed desirable to them to report these cases in order that others with more clinical material may investigate the matter further.

The Intravenous Injections of Small Amounts of Human Blood for the Treatment of Severe Anemias.—WEBER (*Münch. Med. Woch.*, 1913, xl, 1307) suggests the intravenous injection of 5 c.c. of defibrinated human blood for the treatment of cases of severe anemias. The blood is obtained from a healthy donor from six to twenty-four hours before use. He has made forty-six such injections with only very slight reactions following the injection. Weber avoids by these small injections the toxic effects that frequently follow larger amounts, and the therapeutic results have been very good. The technique is much simpler than that for direct transfusion and it seems that the beneficial effects are due not so much to the amount of blood injected as to a stimulating action on the blood forming organs. This treatment should be combined with proper dietetic and hygienic measures and supplemented by arsenic to secure the best results.

One Thousand Subcutaneous Injections of Neosalvarsan.—WECHSELMANN (*Münch. Med. Woch.*, 1913, lx, 1309) writes concerning the subcutaneous use of neosalvarsan. He has given the remedy in this way lately with great success. The technique is described in detail. The injection is given into the area around the great trochanter and great care should be taken that the needle is free and the injection delivered directly over the fascia. The injection must not be made into the fascia, muscle, or subcutaneous fat. This method, while technically more difficult than intravenous or intramuscular injection has, according to Wechselmann, many advantages. There are no untoward by-effects that follow the administration of salvarsan in this way, and it is possible to keep a patient more continuously under the influence of the remedy. If the injection is properly done necrosis does not occur and no more pain results than that which follows intramuscular injections of mercury. Wechselmann gives the remedy in concentrated solution giving from 0.5 to 0.9 gm. of neosalvarsan dissolved in 1 c.c. of freshly distilled sterile salt solution. Neosalvarsan, because of its neutral reaction and non-irritating properties may be given in this way without producing inflammation or necrosis. The remedy is readily absorbed; 75 to 85 per cent. being absorbed in one week, and after six weeks only about 5 per cent. remains unabsorbed.

Amino-acids and Sugar in Rectal Feeding.—SHORT AND BYWATERS (*Brit. Med. Jour.*, 1913, 2739, 1361) review the literature on the subject of rectal feeding and relate their own observations on the absorption of food when introduced in the form of nutrient enemas. They determined the urinary output of total nitrogen and ammonia during periods of fasting followed by periods of rectal feeding. Short

and Bywaters say that the older observations on the absorption of foodstuffs from rectal enemas based on the analysis of rectal "wash outs" are unreliable. The daily output of nitrogen in the urine of patients given nutrient enemas of milk or eggs peptonized for 20 to 30 minutes demonstrates that almost no nitrogenous matter is absorbed. Modern physiological opinion holds that proteins are absorbed principally as amino-acids. The failure of the rectum to absorb ordinary nutrient enemas is largely due to the fact that peptones are given instead of amino-acids. Chemically prepared amino-acids or milk pancreatinized for twenty-four hours so that amino-acids are separated, allows of a much better absorption of nitrogenous foodstuffs from the rectum as demonstrated in five cases by the high nitrogen output in the urine. The low output of ammonia nitrogen shows that the high output was not due to the absorption of putrefactive bodies. The rectal washings were not offensive. Dextrose is much better absorbed than lactose and relieves the acidosis due to starvation. Fat is not well absorbed. Scarcely any of the fat of ordinary milk enemas is retained. The best nutrient enema consists of milk pancreatinized for twenty-four hours, with the addition of 5 per cent. pure dextrose. They consider that the best form of nutrient enema should be prepared as follows: To a pint and a half of milk, boiled and cooled add one half an ounce of some reliable pancreatic fluid or four pancreatic tablets. Keep in the incubator twenty-four hours. Add one half an ounce of pure dextrose. Give five ounces every four hours, or, if the patient can retain it, ten ounces every eight hours.

PEDIATRICS

UNDER THE CHARGE OF

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The Diagnosis and Treatment of Acute Mastoiditis.—GEORGE H. MATHEWSON (*Canadian Med. Assoc. Jour.*, 1913, iii, 672), puts into concrete form the current teachings on this subject. Acute mastoiditis resulting from, or accompanying middle ear disease is the form commonly seen, and as it can often be aborted in its incipient stage its early diagnosis is of vital importance. The presence of an acute or subacute otitis media is almost essential to the development and diagnosis of an acute mastoiditis. The symptoms of acute mastoiditis are tenderness on pressure over the mastoid process, pain in that region, edema and redness of the soft parts behind the auricle, in some cases abscess, prolapse of the posterior superior wall of the membranous meatus near the drum membrane, excessive, creamy, purulent discharge, and elevation of temperature. The most important symptom is tenderness over the mastoid process, especially just behind the external meatus, at the tip of the process, and less frequently about an inch

behind the first point mentioned. Pain in the mastoid is not constant. Edema of the soft parts is frequent but is a late symptom. Furunculosis of the meatus quite as often causes edema here and may simulate mastoid tenderness if the meatus is pulled on while pressure is made over the mastoid. Prolapse of the postero-superior wall of the meatus if present is an indication for operation. If the purulent discharge is great it indicates mastoid involvement. Elevation of temperature is variable and not of much help in diagnosis, as 63 per cent. show a temperature not over 100° F. Prophylaxis is important. In cases of nasopharyngeal inflammation accompanying the exanthemas, cleansing gargles and application of 20 per cent. argyrol should be used. Occurrence of earache in healthy children demands thorough examination of the nose and throat. In existing cases, paracentesis of the drum is very valuable when the membrane is bulging, or if it does not rupture early, or if the existing perforation gives insufficient drainage. A general anesthetic, preferably nitrous oxide gas, should be given in all cases. From 50 per cent. to 75 per cent. of cases if treated early can be aborted by rest in bed, free purgation, establishing good drainage, syringing with hot boric acid solution every two hours, and the application of cold to the mastoid by means of a Leiter's coil. This treatment may be kept up for from twenty-four to forty-eight hours. If there is no marked improvement in forty-eight hours, operation is necessary.

Coli Infection of the Urinary Tract in Childhood.—N. PERCY MARSH (*Brit. Jour. Child. Dis.*, 1913, x, 385) points out that the colon bacillus is usually the cause of cystitis and pyelitis in childhood. Many other organisms such as streptococci, gonococci, staphylococci, etc., occasionally are causal factors. Escherich found the bacillus coli in 58 of a series of 60 cases. Jeffreys reports 67 coli cases out of 121. The difficulty in infants with this condition is in gathering sufficient urine to make a diagnosis, the case often being diagnosed marasmus or tuberculosis. While there is much disagreement on the mode of entry into the urinary tract by the colon bacillus, the fact that 90 per cent. to 95 per cent. of cases occur in girls suggests a direct infection through rectal contamination. The habit of wiping with the diaper from behind forward makes this easy. Another method of infection is from the bowel to the kidney, direct, and many cases do follow ileocolitis, intestinal ulceration, and long-continued constipation. Infection through the blood-stream is another theory. Clinically four conditions are recognized: Bacilluria, the bacilli being found in the mucous clouds formed on standing. Cystitis, in which the urine contains motile organisms and pus cells, and there are dysuria, increased frequency, and slight fever. Pyelitis, in which the constitutional disturbance is greater, with often rigor, shivering, and high, remittent temperature. Lastly, pyelonephritis with severe general symptoms, pronounced wasting, and tube-casts and albumin in the urine besides the bacilli. In infancy the onset is usually sudden, often assuming a remittent type, like enteric, later on. Squint, head-retraction, and drowsiness may simulate meningitis, and local symptoms may be absent altogether. The urine is usually acid, shows a mucous sheen, and has an unpleasant fishy odor. General edema is often one of the

general symptoms. In chronic forms in older children malnutrition is continued, the local symptoms are usually absent, and there is a slight febrile disturbance. The prognosis is variable, the acute cases clearing in one to several weeks, and a considerable number becoming chronic. The condition is rarely fatal. The two chief points in treatment are to ensure a copious secretion of urine, and to render the urine alkaline. The best drug is citrate of potash, 5 to 20 grains every three hours. Bicarbonate of sodium or potassium or sodium citrate may also be used. Urinary antiseptics are used in acute cases, but not in chronic forms. Urotropin being decomposed only in acid urine it is applicable only to chronic cases in which the urine is kept acid. Autogenous vaccines have so far shown little if any result but should be tried as a last resort.

OBSTETRICS

UNDER THE CHARGE OF

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Induced Labor.—The induction of labor by pituitrin was reported by POULIOT and VAYSSIERS (*Bull. de la Soc. d'Obstét. de Paris*, June, 1912). The first dose was 1 c.c., repeated if required, and always given hypodermically. The cases comprised 2 of premature rupture of the membranes, 1 maternal syphilis with retention of a macerated fetus, 3 cases of slight pelvic contraction, and 1 of repeated hemorrhage at about five months. In contraction of the pelvis, the remedy seemed efficient in 2 cases, and useless in 1. When the membranes had ruptured prematurely, labor developed after pituitrin was injected. In a syphilitic patient, pituitrin had no effect. Where the uterus acted, it did so promptly with frequent and intense pain. The normal rhythm was maintained, and the uterus did not show signs of tetanus. Both mothers and children did well in these cases.

The place which induced labor should have in the treatment of contracted pelvis, is discussed by HOFMEIER (*Montasschr. f. Geburts. u. Gynäk.*, Band xxxvi, Festnummer, 1912). In 8000 labors, the induction of labor was practised in 71 cases—68 multiparæ and 3 primiparæ. In the primiparous cases he can give no reason for the induction of labor; 2 of them did well; in the third the child was lost; 16 of these were delivered with true conjugate from 6.5 cm. to 7.5; 43 with true conjugate between 7.5 and 8.5 cm.; and 12 cases where the true conjugate was greater than 8.5 cm. In 68 multiparæ operations were performed on 51 patients. The operation was repeated seventeen times, and in some cases three times upon one patient; 10 children were lost, 14 per cent., and in the first week after labor two others died, but not as the result of labor. This fetal mortality is greatly

lower than that which pertains in contracted pelvis when pregnancy is allowed to go on indefinitely. In regard to primiparæ, he does not believe that labor should be induced after the thirty-sixth week, nor where the true conjugate is less than 7.5 cm. In regard to the results for the mothers, in 71 cases there was no death, while the puerperal period was complicated by morbidity in 17 per cent. Hofmeier concludes from his experience that better results are obtained for mother and child if elective section at the beginning of labor is substituted for the induction of labor. He cites the case of a patient who, after repeated unfortunate and very difficult confinements, had induced labor with the birth of a living child, and who at the next pregnancy requested delivery by section, because it was a much simpler and shorter operation. This he believes will be the attitude of the patients in the future.

BRODHEAD (*Amer. Jour. Obstet.*, May, 1912) reports 139 induced labors with the modified Champetier de Ribes bag. Of these 75 were private, and 64 hospital or out-door patients. There were 48 primiparæ and 91 multiparæ; 75 were at or beyond full term, 53 between eight and nine months, 8 between seven and seven and one-half months, and 3 between six and six and one-half months. The cervix was first dilated by the finger or a steel dilator, and the bag rolled up into as small a bulk as possible was passed into the cervix and slowly filled with 1 per cent. lysol or salt solution. The stem was then clamped and tied. Bags No. 2 and No. 3 were used most frequently. In 4 of these cases, the membranes had ruptured, and, in 6, the membranes were accidentally ruptured during manipulation. The length of labor varied in primiparæ from two hours and fifty minutes to seventy-nine hours and fifty-two minutes, the average being twenty-two hours and nine minutes. In multiparæ, the average duration of labor was fifteen hours and fifty-two minutes. Labor terminated spontaneously in 49 per cent.; with low forceps in 21 per cent.; with medium forceps in 11 per cent.; with high forceps in 3 per cent. Version was employed in 10 per cent., breech extraction in 3 per cent., craniotomy in 1 per cent., Cesarean section in 1 per cent.; and 1 patient, or 1 per cent. of all, died undelivered. Presentation of the child was changed in 7 cases, or 5 per cent., but in only 1 of these was the final result of labor altered.

BAGGER-JÖRGENSEN (*Monatsschr. f. Geburts. u. Gynäk.*, 1912, Band xxxvi, Heft 1) states that the opposition to the induction of labor for contracted pelvis is usually based upon the fetal mortality. It has been his practice not to induce labor if the true conjugate was less than 8.5 cm.; thus, in 6400 labors, the operation was performed in 29 cases, among 100 cases of contracted pelvis. From the thirty-fifth to the thirty-eighth week was the time chosen, with but 3 exceptions, 1 in the thirty-fourth week and 2 in the thirty-seventh week. In the majority, the bougie was used to excite labor pains, and in one patient it was necessary to introduce the bougie fourteen times before labor developed. The pains occurred in from fifteen minutes to eight days, usually in sixty hours after the first bougie was inserted. On account of the delay occasioned by this method, in the last 4 patients labor was induced by rupturing the membranes. Pains developed within thirty-two hours afterward, and the actual duration of labor was reduced

to thirteen hours. The birth was spontaneous. Where bougies were used labor lasted twenty-one hours; 63.4 per cent. of the children were born spontaneously. There was no maternal mortality, but 3 of the children died during labor—a primary mortality of 10 per cent. In one of these cases the cord prolapsed; in one case the bougie wounded the placenta, causing hemorrhage; and in one case the child died from asphyxia. The best time, in his opinion, for the operation, is the thirty-fifth week, and among his cases 90 per cent. of the children were discharged from hospital with the mothers living. During the first year of life among these children, the mortality was 8 per cent., or during the first two years, in all, 12 per cent.

UDACTA (*Rev. de Medicina y. Cirurgia Practicas*, October 14 and 28, 1912) publishes 2 cases reported at the Spanish Gynecological Society, where pituitrin was used in the treatment of uterine hemorrhage. The first patient was two months pregnant, having hemorrhage with clots and pieces of substances which apparently were placenta. On the third day after the first visit she had a hemorrhage, for which a hypodermic injection of pituitrin was given. Pain developed with the expulsion of a quantity of blood from the uterus, and about three-quarters of an hour later a blood clot and mass of placenta. The patient's symptoms speedily subsided and she made a complete recovery without further treatment. In the second case reported, the placenta was retained, and before proceeding to manual delivery pituitrin was given hypodermically. This caused the uterus to act and the placenta was expelled. The Society discussed the paper, and Botin reported 4 cases, in 3 of which the result was prompt and satisfactory, while in the fourth case pituitrin failed to produce uterine contractions. In the discussion, Botin spoke of the difficulty of removing the pituitary gland in the living animal. The interference required is so extensive that it is difficult to isolate the effect of the operation from the results produced by the ablation of the gland. A recent method by which the gland is removed through the orbit produces less traumatism and may improve the results. The action of pituitrin on the uterine muscle is in the beginning of its effect tetanic. This is followed by contractions like those of normal labor. Smaller doses are not efficient, and produce somewhat of the tetanic effect. The patient quickly becomes accustomed to its use, so that injections after the first, act with progressively less effect. With this in view, it is wise to reserve pituitrin for a decided emergency where immediate uterine contraction is essential. As it seems to enhance the normal action of the uterus, it can be used for inertia, and may obviate the necessity for forceps delivery. Others in discussion found that secondary relaxation of the uterus might produce hemorrhage. To avoid this, it seems best to use repeated injections. It is essential that the exact cause of delayed labor should be made out, as if pituitrin were used where an insurmountable obstacle to parturition was present, the results would, of course, be disastrous.

GYNECOLOGY

UNDER THE CHARGE OF

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Female Labor and Gynecological Diseases.—A paper of considerable sociological interest has recently been published by HIRSCH (*Monat. f. Geb. u. Gyn.*, 1913, xxxviii, Ergzhft., 198), drawing attention to the steady increase in the proportion of women who are engaged in some regular occupation outside their homes, as a result of which they are constantly subjected to conditions more or less inimical to health, which in former times were practically unknown. The demands made upon the female organism by the bearing and rearing of children remain unchanged, however, and thus, Hirsch believes, arise in many instances pathologic conditions which, taken in the aggregate, are becoming of the greatest social as well as individual significance. Thus, work done constantly in a sitting posture causes pressure on the lower abdominal organs, resulting in inhibition of circulation and impaired digestive activity. Long standing, as is required in certain occupations, leads to increased intra-abdominal pressure, hernia, prolapse, and venous congestion in the lower extremities. Work in a more or less bent over posture often results in spinal curvatures, hernia, prolapse, possibly also renal and vesical disorders. In many industries, women are brought into constant contact with injurious substances, such as atmospheric impurities, dust, noxious gases, metallic or other poisons, bacteria, etc. The importance of these conditions from the gynecologist's point of view lies primarily in the fact that the genital organs, perhaps more than any others in the female body, are affected by any impairment of general constitutional tone, and deleterious influences are therefore apt to show their effects first in this sphere. With regard to specific industries, Hirsch has found that laundresses, seamstresses, textile workers, and clerks are especially prone to anemia and chlorosis, conditions which are often the direct precursors of tuberculosis, with all its serious effects upon pregnancy and labor. The records of the large Leipzig "Krankenkasse" show that abortion occurs about 7 times as frequently in working as in non-working women, premature labor 6 times, and various accidents of pregnancy (such as placenta prævia, hyperemesis, hemorrhage, extra-uterine gestation, etc.) about 3 times as frequently in the former as in the latter class. In certain industries, also, such as pottery manufacture, printing, straw hat bleaching, glass making, and in some textile branches, lead salts are employed, and it has been found that women employed in these trades are especially prone to premature labors and still births. This condition is apparently due to a toxic influence upon the maternal organism; not only does the lead pass through the placenta as has been proved by its presence in fetal organs, but it can be demonstrated in the mother's milk, and may thus lead to poisoning of infants born

alive. Similar conditions are found to a greater or less extent among women employed in all sorts of metal industries. In many occupations, such as copper working, dyeing, the manufacture of carpets, artificial flowers, toys, glassware, etc., chronic arsenic poisoning occurs, often entirely unsuspected, and gives rise to stubborn, deep ulcers on the genitalia; somewhat similar pathologic lesions are seen in women subjected to the influence of mercury, as in chemical works, the manufacture of mirrors, etc. In spinning and weaving establishments young women and girls are employed in large numbers, this work often resulting in stunted or deformed growth. In tobacco factories, in which a particularly large proportion of the workers are women, menstrual anomalies, cervical catarrh, and metritis are abnormally common. It has been shown statistically that women employed in all these industries have a higher percentage of sickness, and also a higher death rate, than do men of the same age employed in the same occupations, and numerous other forms of work exert likewise more or less specific effects upon the health of their female employees. Hirsch emphasizes the fact that this is a field of investigation which has as yet barely been entered upon, but which must in the near future receive thorough scientific consideration. Deleterious influences, such as have been spoken of, menacing a large and ever-increasing proportion of the female population, are of the utmost gravity, and require, in his opinion, the institution of energetic measures on the part of the state.

Menstrual Fever in Pulmonary Tuberculosis.—WEISE (*Beitr. z. Klinik d. Tuberculose*, 1913, xxvi, 336), has made careful temperature measurements every two hours during the day over periods of several months, using as subjects 500 tuberculous women under sanitarium treatment, all of whom gave a positive tuberculin reaction, and most of whom had demonstrable tubercle bacilli in the sputum. He found a *premenstrual* rise of temperature in 201 cases (40 per cent.); in some instances this seemed to be distinctly associated with an aggravation of the patient's symptoms, in others, however, it appeared to be purely psychic. Fever *during* the period was present in 68 cases (13.6 per cent.). Although in a majority of these, the rise of temperature was slight, in a few it was quite marked, and was accompanied by severe constitutional symptoms. In 12 cases (2.4 per cent.) the temperature was normal before and during menstruation, but was elevated in the first few days *after* the termination of the period. In all these patients, however, the rise was slight, and of apparently little significance. There were 58 cases (11.6 per cent.), on the other hand, in which the temperature had been for some time above normal, but *fell* with onset of menstruation. In some instances, this fall was noticed only during one period, in others the fever did not recur. Weise thinks that this phenomenon may possibly be due to a favorable influence exerted on the pulmonary condition by the general hyperemia associated with menstruation. In the remaining 161 cases (32.2 per cent.) there was no noticeable change in the temperature before, during, or after the menstrual period. It would appear from these observations, therefore, that there is no *typical* form of thermic disturbance associated with menstruation in tuberculous subjects, but Weise does believe that the menstrual period on such women is a particularly critical

time, during which they should be very careful to avoid the slightest exposure to cold, over-exertion, or other upsetting influences. He thinks moreover, that if in any woman a regular rise of temperature occurs at each menstrual period, the suspicion should be aroused of the possible existence of a tuberculous focus somewhere in the body, most probably in the lungs.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF
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Fracture of the Base of the Cranium as a Cause of Paralysis of the Palate, the Larynx, and the Shoulder.—SIEBENMANN (*Annales des Maladies de l'Oreille, du Lar., du Nez, et du Pharynx*, January, 1913) states that fracture of the base of the cranium may involve the nerves which supply the soft palate and the larynx, and likewise the accessory nerve which innervates the muscles of the shoulder. There may even be a lesion of the hypoglossal nerve as indicated by paralysis of the tongue. The lesion is usually due to a blow on the head which produces a fracture involving the region of the jugular foramen, and directed most frequently toward the sella turcica, and sometimes toward the pyramid.

Paraffin Injections into Paralyzed Vocal Cords.—BRUNINGS (*Annales des Maladies de l'Oreille, du Lar., du Nez, et du Phar.*, January, 1913) reports eight cases of vocal failure due to paralysis of the recurrent nerve, treated by the injection of paraffin into the paralyzed vocal cord. The injection is made by the direct method, and the paraffine must not be too hard.

On the Treatment of Vegetant Tuberculous Laryngitis.—CANESTRO (*Annales des Maladies de l'Oreille, du Lar., du Nez, et du Pharynx*, March 3, 1913), utilizing the necrosing action and slow cauterization of neutral quinia hydrochlorate, employed this drug in a typical case of vegetant tuberculosis laryngitis, and obtained transformation of this lesion into an infiltrated ulceration of good aspect, much more apt to succumb to the successful action of the usual remedies.

The Anesthesia for Bronchoscopy.—EPHRAIM (*Annales des Maladies de l'Oreille, du Lar., du Nez, et du Phar.*, January, 1913) replaces cocaine anesthesia for the larynx with a solution of 20 per cent. alypin, of which one part is mixed with three parts of adrenalin solution, 1 to 1000. For anesthesia of the trachea and the bronchi Ephraim uses a solution of the double salt of quinine and urea in the strength of 1

per cent. only, which produces a rapid and sufficient anesthesia, permitting not only the introduction of the tube but endobronchic intervention also. This solution is perfectly innocuous, and may be employed without any dread.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Roaches.—J. FIBIGER (*Berl. klin. Woch.*, February 17, 1913, No. 7, p. 289) has shown that roaches may become infested with a round worm, a new species of the genus *spiroptera*. When these infested roaches are eaten by rats (*Mus decumanus*), a cancerous-like growth develops in the stomach of the rats, presumably due to the irritating presence of these worms. The egg of the worm is passed in the feces of the rat, and the life cycle is completed by the roaches eating the eggs. Fibiger found tumors in only 11 out of 1144 rats caught in Copenhagen. On the other hand, out of 61 rats caught in the location of a sugar refinery, he found the worms in the stomach of 40, and pathological changes in the nature of a carcinomatous overgrowth in 18. Attention is drawn to the relation between this endemicity of the affection in rats and the supposed endemicity of cancer in man. The tumor-like overgrowth in the stomach of the rat is of the squamous epithelial type. Metastases sometimes occur. The rats cannot be infected by feeding them with the eggs of the worm; they must ingest the larvæ which occurs in the infested roach. Attention is drawn to a number of other investigators who have noted a relation between parasites, such as trichinæ, bilharzia, and flukes with human cancer. HERMS and NELSON (*Am. Jour. of Pub. Health*, September, 1913, iii, No. 9, p. 929), also LONGFELLOW (*Am. Jour. of Pub. Health*, January, 1913, iii, No. 1, p. 58), have shown the possibility of the conveyance of typhoid bacilli and other infections by means of the roach. When we consider that roaches feed upon all kinds of breadstuffs, milk and its products, meat, clothing, cooked and raw foods; that they migrate from one apartment to another, following water and drain pipes; that they come from cellar and sickroom to living rooms and bedrooms; and that they overrun pantries, kitchens, and storerooms, opportunity is evidently offered to drag infection mechanically from one place to another. The roach is, therefore, under the suspicion of being a sanitary menace.

Ozone.—E. O. JORDAN and A. J. CARLSON (*Jour. Am. Med. Assoc.*, September 27, 1913), studied the bactericidal, physiologic and deodor-

izing action of ozone, and W. A. SAWYER, HELEN L. BECKWITH, and ESTHER SKOLFIELD (*Jour. Am. Med. Assoc.*, September 27, 1913) studied the alleged purification of air by the ozone machine. These two very important articles agree in their conclusions, to wit, that although some bacteria, especially if in a moist condition, may be killed by ozone, the amount necessary for this bactericidal action is so great as to affect injuriously human beings. As a disinfectant, formaldehyde is much more efficient. Ozone may mask odors, but the deleterious action of the ozone on the respiratory tract is of greater moment than the odor itself. The ozone machine should not, therefore, be allowed in schools, offices, or other places in which people remain for considerable periods of time. The machines conceal faults of ventilation rather than correct them.

Beriberi in the Amazon Valley not Due to Polished Rice.—LOVELACE (*Amer. Jour. Tropical Diseases and Preventive Medicine*, August, 1913, i, No. 2, p. 140) reports the prevalence of a polyneuritis which is both clinically and anatomically indistinguishable from beriberi of the Orient. This disease is not associated with a rice diet and it is not due to the absence of any of the recognized food elements. It occurs in well-fed, non-rice-eating young adults, and presents a mortality of 15 to 20 per cent. Clinically there are two types, first, the cardiovascular type, in which circulatory symptoms, tachycardia, dyspnea, edema predominate; second, the paralytic type, in which paralysis of the various muscles with areas of abnormal sensation is the characteristic feature. Very often these two types occur together. Lovelace reviews the work of Fraser and Stanton, Strong and Eijkman, all of whom have shown that a diet of polished rice will cause polyneuritis. He accepts their conclusions but points to polished rice as only one etiological factor. His conclusions are: (1) Among the 963 cases of beriberi to which reference is made, were many in which the factors of defective diet and of a rice diet could be positively and definitely excluded. This is in line with the reports of many observers in many parts of the world. (2) The experiments of Fraser and Stanton, confirmed by other workers, are conclusive to the effect that the beriberi symptom-complex may be induced by a diet of polished rice. (3) As a corollary from these two conclusions and considering the multiplicity and diverse characters of the agents that are known to cause multiple neuritis, it is highly probable that the term "beriberi" is one that has been used to cover not a single disease, but a group of diseases, more or less indistinguishable clinically. (4) The question of the etiology of beriberi cannot yet be regarded as settled.

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All communications should be addressed to—

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